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## AND GENETIC TESTING FOR ALL . . . THE COMING REVOLUTION IN NON-INVASIVE PRENATAL GENETIC TESTING

*Jaime S. King\**

For thousands of years, expecting parents have daydreamed of being able to know about their children before their birth. Over the last thirty years, reproductive genetics and assisted reproductive technology (ART) have made significant strides toward fulfilling this desire. A steady stream of technical advances including prenatal screening, invasive prenatal diagnosis, sperm and egg donation, sperm sorting for gender selection, in vitro fertilization, and preimplantation genetic diagnosis have sought to give parents more information about and control over their reproductive practices. However, each of these technologies has significant drawbacks that limit its use to either a very small population or a small number of conditions. As a result, their overall impact on reproduction has been equally limited.<sup>1</sup>

Everything is about to change. Scientists have recently discovered a way to provide diagnostic genetic information to pregnant women early in

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1. Although, non-medical sex selection through sperm sorting, ultrasound sex determination and preimplantation genetic diagnosis have had a significant impact on the male to female ratio in society in countries like India and China with strong preferences for male offspring.

pregnancy through a blood test, which poses no risk to the fetus. Researchers have long sought a test that offers non-invasive prenatal genetic diagnosis (NIPD). NIPD was finally achieved by capturing and analyzing fragments of fetal DNA, known as cell-free fetal DNA (cffDNA), found in the pregnant woman's bloodstream.<sup>2</sup> By examining cffDNA, scientists have been able to detect a wide range of known genetic and chromosomal conditions with a high degree of accuracy.<sup>3</sup> Existing cffDNA clinical applications include testing for Down syndrome, trisomy 13, trisomy 18, fetal sex, and potential pregnancy complications, such as an Rh factor incompatibility.<sup>4</sup> However, the future promises testing for single gene disorders and more complex genetic diseases and conditions, culminating in the possibility of conducting genome wide analysis of the complete fetal genome using cffDNA from a maternal blood sample.<sup>5</sup> In December 2010, two separate laboratories demonstrated that a full genome-wide analysis of the fetus could be performed from a sample of the mother's blood, making prenatal testing for any diagnosable genetic condition or predisposition possible in the future.<sup>6</sup>

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2. Y.M. Dennis Lo et al., *Presence of Fetal DNA in Maternal Plasma and Serum*, 350 LANCET 485, 485–87 (1997) [hereinafter Lo et al., *Presence of Fetal DNA*]; Y.M.D. Lo, *Non-invasive Prenatal Detection of Fetal Chromosomal Aneuploidies by Maternal Plasma Nucleic Acid Analysis: A Review of the Current State of the Art*, 116 BRIT. J. OBSTETRICS & GYNAECOLOGY 152, 152 (2009) [hereinafter Lo, *Non-invasive Prenatal Detection*].

3. *Id.*; Y.M. Dennis Lo et al., *Maternal Plasma DNA Sequencing Reveals the Genome-Wide Genetic and Mutational Profile of the Fetus*, 2 SCI. TRANSLATIONAL MED. 1 (2010); Mei-Chi Cheung et al., *Prenatal Diagnosis of Sickle Cell Anemia and Thalassemia by Analysis of Fetal Cells in Maternal Blood*, 14 NATURE GENETICS 264, 264–68 (1996); H. Christina Fan et al., *Non-invasive Diagnosis of Fetal Aneuploidy by Shotgun Sequencing DNA From Maternal Blood*, 105 PROC. NATL. ACAD. SCI. 16266, 16266 (2008). These tests are able to detect the genetic or chromosomal variables associated with the disorder with a high degree of accuracy. However, other factors like penetrance, gene-gene, and gene-environment interactions may affect the likelihood of the child manifesting the physical symptoms of disease.

4. *Sequenom CMM's MaterniT21 PLUS Test Expands Current Prenatal Testing Offering*, SEQUENOM.COM (Feb. 8, 2012) <http://sequenom.investorroom.com/index.php?s=43&item=326>; *Verinata Health Announces Presentation and Publication of Top-Line Clinical Validation Study Results for its veriFi™ Non-Invasive Prenatal Test*, VERINATA.COM, <http://www.verinata.com/news/non-invasive-prenatal-test/> (last visited Mar. 20, 2012); Caroline F. Wright & Hillary Burton, *The Use of Cell-free Fetal Nucleic Acids in Maternal Blood for Non-invasive Prenatal Diagnosis*, 15 HUM. REPRODUCTION UPDATE 139, 142 (2009).

5. Lo et al., *supra* note 3, at 3; H. Christina Fan & Stephen R. Quake, *In Principle Method for Non-invasive Determination of the Fetal Genome*, NATURE PRECEDINGS (Dec. 8, 2010), doi:10.1038/npre.2010.5373.1.

6. The two laboratories were at Stanford University and the Chinese University of Hong Kong. The Stanford lab is run by Stephen Quake and commercially associated with

Manifesting this technological potential will offer prospective parents a risk-free and relatively inexpensive means to discover an enormous amount of information about their fetus at a very early point in the pregnancy, which will be limited only by our knowledge and understanding of genetics. NIPD using cffDNA is currently offered as early as nine weeks gestation and is less expensive than current prenatal testing methods.<sup>7</sup> Once successfully commercialized and integrated into practice, NIPD testing for a range of genetic disorders and conditions is well poised to become the standard of care, such that it would be routinely offered to all pregnant women.

Without question, the availability of NIPD through the use of cffDNA testing marks an enormous advance in reproductive genetic testing that will provide significant benefits to millions of prospective parents, but it does not come without challenges and complications. NIPD promises to expand our ability to provide pregnant women with genetic information about their fetuses, but in many cases, it will not improve our ability to explain the implications of much of that information in a meaningful way. Often physicians themselves do not fully understand the results of a genetic test, or are not well trained in how to communicate those results to patients. Further, while the majority of existing genetic tests examine disorders that arise from a mutation in a single gene, the vast majority of heritable conditions and traits result from the interactions of multiple genes or genes and the environment. For these conditions, NIPD testing will most likely provide prospective parents with a series of probabilities that a fetus will have a specific condition or characteristic. In order for NIPD to truly improve reproductive decision making, physicians and pregnant women will need guidance on which tests are appropriate for prenatal use, how to determine what tests each woman would like to receive, how to interpret the results, and finally, what options are available after testing. Given NIPD's recent arrival, we should take steps to address the initial challenges to its integration into prenatal practice and begin to discuss the broader implications of widespread NIPD use.

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Verinata. The one at the Chinese University of Hong Kong is run by Dennis Lo and commercially associated with Sequenom. Lo et al., *supra* note 3, at 1; Fan & Quake, *supra* note 5.

7. *Sequenom Center for Molecular Medicine Announces Launch of MaterniT21™ Noninvasive Prenatal Test for Down syndrome*, SEQUENOM.COM, (Oct. 17, 2011), <http://sequenom.investorroom.com/index.php?s=43&item=310>; Caroline Wright, *Cell-Free Fetal Nucleic Acids for Non-Invasive Prenatal Diagnosis, Report of the UK Expert Working Group*, PHG FOUNDATION, 13, 23 (2009), available at [http://www.phgfoundation.org/download/ffdna/ffdna\\_report.pdf](http://www.phgfoundation.org/download/ffdna/ffdna_report.pdf).

This Article examines a range of ethical, legal and social implications associated with introducing NIPD into prenatal practice, and offers a novel solution to assist physicians and patients in making informed choices regarding reproductive genetic testing. Part I describes the current status of NIPD and compares it to existing reproductive genetic testing technologies. Specifically, Part IA describes the development of cfDNA technology and its current and potential uses for NIPD, including identification of potential pregnancy complications, fetal sex determination, chromosomal testing, testing for single gene disorders, and whole genome screening. Readers less interested in the technical details of NIPD may wish to move quickly through IA ahead to Part IB. Part IB argues that NIPD has three features that differentiate it from existing reproductive genetic testing techniques in ways that are critical. First, it is non-invasive, and therefore presents no physical risk to the fetus or mother. Second, NIPD can be offered soon after a woman discovers she is pregnant. Third, over time it will be comparatively less expensive than existing prenatal screening and diagnosis techniques.

Part II then explores how a prenatal genetic test with these characteristics will affect reproductive practices and overall prenatal care. Specifically, the Article analyzes how NIPD will impact who receives reproductive genetic tests, what tests are offered, and what role they play in reproductive decisions. I then argue that the introduction of NIPD into prenatal practice will significantly increase the number of women who will receive prenatal genetic diagnosis, broaden the scope of conditions and characteristics they test for, and offer this information to parents at a point in the pregnancy when it is more actionable.

Next, Part III addresses the initial challenges of offering a large amount of information routinely to pregnant women at a very early point in the pregnancy. As NIPD is integrated into prenatal practice, physicians will face many challenges regarding what tests to offer and what information to provide patients. For the most part, these challenges are due to an absence of regulation and guidance regarding the appropriate uses of prenatal genetic tests. In addition, NIPD will strain current genetic counseling and informed consent protocols. The Article argues that a new method of informing patients about the prenatal genetic tests offered through NIPD is required in order for physicians to meet their informed consent obligations. It also discusses the potential emotional and psychological harms that can arise for women if the informed consent process is not performed appropriately, causing them to receive diagnostic genetic results that they did not knowingly want, or worse, that they knowingly did not want. To remedy these issues, Part III proposes the use of a two-step informed consent process that offers pregnant women a variety of genetic testing panels. Each panel

will consist of multiple genetic conditions with similar salient clinical features, such as severity of symptoms, age of onset, and likelihood of contracting the disease. This approach aims to simplify the genetic counseling requirements, ease the regulatory approval process, and permit physicians to use advances in informed consent technology, like decision aids, to improve the decision-making process for both parents and physicians.

Finally, Part IV will highlight some potential societal issues that may be raised by the advent of widespread cffDNA testing. Full analysis of the topics in Part IV is beyond the scope of this Article, but the topics are mentioned to encourage future discussion, research and writing on the long term implications of widespread NIPD use.

## I. NON-INVASIVE PRENATAL GENETIC DIAGNOSIS VIA CELL FREE FETAL DNA

### A. *The Development of NIPD*

For the last three decades, scientists have known that whole fetal cells pass through the placenta into pregnant women's blood.<sup>8</sup> This discovery opened the possibility of obtaining fetal DNA from maternal blood, which would provide a much sought after non-invasive testing option for reproductive genetic testing.<sup>9</sup> Current methods of diagnostic prenatal genetic testing carry around a 1 percent risk of fetal miscarriage and can be quite uncomfortable for the pregnant woman.<sup>10</sup> However, producing a commercially viable, non-invasive, prenatal genetic test from fetal cells in the mother's blood has remained elusive due to technical challenges.<sup>11</sup>

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8. Leonard A. Herzenberg et al., *Fetal Cells in the Blood of Pregnant Women: Detection and Enrichment by Fluorescence-activated Cell Sorting*, 76 PROC. NAT'L ACAD. SCI. USA 1453, 1453–55 (1979); Cheung, *supra* note 3 at 264–68; Fan et al., *supra* note 3 at 16266.

9. Cheung, *supra* note 3 at 264–68.

10. Caroline F. Wright & Lyn S. Chitty, *Cell-free Fetal DNA and RNA in Maternal Blood: Implications for Safer Antenatal Testing*, 339 BRIT. MED. J. 161, 161 (2009).

11. Difficulties have occurred on two fronts. First, whole fetal cells are difficult to find in the mother's blood. See Diana W. Bianchi et al., *PCR Quantitation of Fetal Cells in Maternal Blood in Normal and Aneuploidy Pregnancies*, 61 AM. J. HUM. GENETICS 822 (1997); Lo, *Non-invasive Prenatal Detection*, *supra* note 2, at 152. Second, while rare, these cells can live in maternal blood for decades, meaning that a geneticist would not know if the cell found was from the existing pregnancy or a former one. See Wright & Burton, *supra* note 4, at 142 (2009). In 2002, a multicenter trial, using the some of the best technology for the

Researchers have since found an alternative path to non-invasive testing using DNA that floats freely in maternal blood. In 1997, Dennis Lo and colleagues, researchers from The Chinese University of Hong Kong, discovered that fragments of DNA from a fetus exist outside the cell in the blood plasma of its mother.<sup>12</sup> During pregnancy, this cell-free fetal DNA (cffDNA) represents anywhere from 3 to 10 percent of the cell free DNA in the maternal blood stream, with the remaining 90 to 97 percent belonging to the mother.<sup>13</sup> Cell-free fetal DNA is typically found in short fragments,<sup>14</sup> and can be detected as early as four weeks gestation.<sup>15</sup> However, the concentration of cffDNA increases with gestational age until seven weeks when it stabilizes at about 10 percent for the remainder of the pregnancy.<sup>16</sup> After the birth, cffDNA clears from the maternal blood within two hours, ensuring that any fetal DNA detected is from the current fetus.<sup>17</sup> Over the last decade, these findings have dramatically changed the landscape with respect to the possibilities for prenatal genetic diagnosis.<sup>18</sup>

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isolation of nucleated fetal cells from maternal blood, reported a sensitivity of only 41.4 percent for the detection of male fetal cells in maternal blood, with a false positive rate of 11.1 percent. D. W. Bianchi et al., *Fetal Gender and Aneuploidy Detection Using Fetal Cells in Maternal Blood: Analysis of NIFTY I Data*, 22 *PRENATAL DIAGNOSIS* 609, 609 (2002). Sensitivity is the ability of a test to correctly identify positive responses, i.e. the true positive rate. As a result of this and other similar research findings, scientists have not successfully commercialized a genetic test based on whole fetal cells in maternal blood.

12. Lo et al., *Presence of Fetal DNA*, *supra* note 2, at 485–87.

13. Lo, *Non-invasive Prenatal Detection*, *supra* note 2, at 153 (stating that cffDNA makes up a mean of 3–6 percent of DNA present in maternal plasma); Fan et al., *supra* note 3, at 16266 (stating that fetal DNA can constitute up to 10 percent of the total cell free DNA in the maternal serum); Fiona M. F. Lun et al., *Non-invasive Prenatal Diagnosis of Monogenic Diseases by Digital Size Selection and Relative Mutation Dosage on DNA in Maternal Plasma*, 105 *PROC. NATL. ACAD. SCI.* 19920, 19920 (2008).

14. K.C. Allen Chan et al., *Size Distributions of Maternal and Fetal DNA in Maternal Plasma*, 50 *CLINICAL CHEMISTRY* 88, 88 (2004).

15. S. Illanes et al., *Early Detection of Cell-free Fetal DNA in Maternal Plasma*, 83 *EARLY HUM. DEV.* 563, 565 (2007).

16. Lyndsey Birch et al., *Accurate and Robust Quantification of Circulating Fetal and Total DNA in Maternal Plasma From 5 to 41 Weeks of Gestation*, 51 *CLINICAL CHEMISTRY* 312 (2005).

17. Lo, *Non-invasive Prenatal Detection*, *supra* note 2, at 153; Y.M. Dennis Lo et al., *Rapid Clearance of Fetal DNA From Maternal Plasma*, 64 *AM. J. HUM. GENETICS* 218 (1999).

18. However, the road to producing a commercially viable NIPD test has not been easy. Four major challenges arose: (1) low concentration of all cell free DNA in blood; (2) total amount of cell free DNA varies significantly from individual to individual; (3) the ratio of maternal cell free DNA to cffDNA molecules is high; and, (4) half of the fetal genome is from the mother. Wright & Burton, *supra* note 4, at 140. To address these issues, researchers must purify and isolate cell free DNA from maternal blood plasma and then compare known

Initial uses of cffDNA include diagnostic testing for the potential pregnancy complications (such as an Rh factor incompatibility), sex of the fetus, single gene disorders, and chromosomal disorders (including Down syndrome).<sup>19</sup> In the future, researchers plan to develop tests for more complex genetic diseases and conditions, culminating in the possibility of conducting genome wide analysis of the complete fetal genome using cffDNA from a maternal blood sample.<sup>20</sup> Realizing this potential will offer prospective parents an enormous amount of information about their fetus, limited only by our understanding of genetics. Each of these uses will be discussed in more depth below.

### 1. Pregnancy Complications

Cell-free fetal DNA testing can diagnose two kinds of conditions during pregnancy that affect maternal-fetal wellbeing: abnormal placental functioning and fetal Rhesus blood group incompatibility.<sup>21</sup> First, elevated levels of cffDNA in the mother's blood can signal an increased risk of a variety of pregnancy complications, especially those associated with abnormal formation or function of the placenta.<sup>22</sup> Such complications include preeclampsia (the leading cause of premature birth and the most common dangerous complication of childbirth), preterm labor, severe morning sickness, intrauterine growth restriction, fetomaternal hemorrhage, and polyhydramnios (too much amniotic fluid).<sup>23</sup> Identifying these complications early in pregnancy, even before symptoms arise, can improve prenatal healthcare outcomes for both the mother and child.

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genetic markers and polymorphisms to differentiate between maternal cell free DNA and cffDNA. *Id.* A number of different methods have been used to differentiate between maternal and fetal DNA including real-time quantitative PCR, nested PCR, digital PCR, gel electrophoresis, and mass spectrometry. *Id.* at 141. The ratio of maternal to fetal cell free DNA can also be improved by using standard size fractionation or mass spectrometry to select smaller DNA fragments that are more likely to have come from the fetus. *Id.*

19. Wright & Burton, *supra* note 4, at 142.

20. Lo, *Non-invasive Prenatal Detection*, *supra* note 2; Fan & Quake, *supra* note 5.

21. Wright & Burton, *supra* note 4, at 144.

22. *Id.* at 145.

23. *Id.*; S. Hahn et al., *Fetal Cells and Cell Free Fetal Nucleic in Maternal Blood: New Tools to Study Abnormal Placentation?*, 26 *PLACENTA* 515 (2005). Although researchers have discussed using cffDNA concentration as another biomarker during pregnancy to detect preeclampsia in asymptomatic patients, due to cffDNA's constant concentration fluctuations, challenges with diagnostic accuracy must be overcome prior to widespread use of a screening test. Wright & Burton, *supra* note 4, at 145.



Second, the availability of NIPD through cffDNA testing can eliminate unnecessary treatments in many pregnant women. For example, cffDNA testing can provide information on the Rh status of a fetus in a non-invasive manner. The presence or absence of Rhesus D (RhD) antigens on the surface of blood cells determines the positive or negative designation in an individual's blood type.<sup>24</sup> Problems arise when Rh-positive fetal blood cells carrying paternally inherited RhD antigens enter an Rh-negative mother's blood stream during delivery, which does not have the RhD antigens. In that case, the Rh-negative mother will produce an immune response against the "foreign" fetus.<sup>25</sup> This immune response will not harm the first fetus during delivery. But if another child is conceived with RhD antigens, maternal antibodies can cross the placenta and attack the new fetus' red blood cells, which can be fatal to the fetus.<sup>26</sup> Rh incompatibility can be treated prophylactically with anti-D antibodies during pregnancy. Unfortunately, current methods of prenatal diagnosis are invasive and have additional risks beyond the 1 percent increase in miscarriage when testing for RhD status, making it risky to identify an at-risk pregnancy.<sup>27</sup> As a result, all women with prior Rh incompatible children are put on prophylactic anti-D antibodies during their subsequent pregnancies.<sup>28</sup> Cell-free fetal DNA provides a powerful tool to safely and easily identify only those fetuses with an incompatible Rh status, thereby eliminating unnecessary treatment of all women with a prior Rh incompatible pregnancy.<sup>29</sup> Rh status testing is one of the first commercialized clinical applications of cffDNA testing.

## 2. Fetal Sex Determination

Geneticists first used cffDNA to detect major similarities or differences between the fetal and maternal DNA, such as the sex of the fetus.<sup>30</sup> In the

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24. Wright & Burton, *supra* note 4, at 145.

25. Am. College of Obstetricians and Gynecologists, Practice Bulletin No. 75: management of alloimmunization, 108 OBSTETRICS & GYNECOLOGY 457-64 (2006).

26. Wright & Burton, *supra* note 4, at 144.

27. Richard B. Smith et al., *The Obstetrician's View: Ethical and Societal Implications of Non-Invasive Prenatal Diagnosis*, 26 PRENATAL DIAGNOSIS 631, 631 (2006). The additional risks include fetomaternal hemorrhage and conversion of mild to severe rhesus hemolytic disease. *Id.*

28. Wright & Chitty, *supra* note 10, at 162.

29. Wright & Burton, *supra* note 4, at 144; Ossie Geifman-Holzman et al., *Diagnostic Accuracy of Non-invasive Fetal Rh Genotyping From Maternal Blood—A Meta-analysis*, 195 AM. J. OBSTETRICS & GYNECOLOGY 1163, 1164 (2006).

30. Lo, *Non-invasive Prenatal Detection*, *supra* note 2, at 153.

case of sex determination, the presence or absence of a Y chromosome reveals fetal sex. If cffDNA from the Y chromosome is present the fetus is male, if not, female. In families with a history of X-linked disorders, such as Duchenne/Becker Muscular Dystrophy, sex determination provides a powerful tool for identifying male fetuses at risk for the X-linked disease.<sup>31</sup> Of course, scientists can also use such testing capability to determine the sex of the fetus for non-medical purposes, such as family balancing or parental preference. A handful of biotechnology companies already offer cffDNA testing for fetal sex determination on a direct-to-consumer (DTC) basis.<sup>32</sup>

### 3. Single Gene Disorders

Researchers can also use cffDNA to detect any paternally inherited or spontaneously occurring genetic mutations, which would not be present in the mother's DNA.<sup>33</sup>

Thousands of genetic diseases result from a mutation in a single gene, often at a single locus.<sup>34</sup> Due to the fragmented nature of cffDNA, detecting both large-scale mutations and single point mutations has been very challenging and generally limited to only the detection of alleles not present in the mother.<sup>35</sup> However, researchers are making rapid progress in this area. For autosomal dominant disorders, like Huntington's disease<sup>36</sup> and Achondroplasia,<sup>37</sup> in which receiving one copy of the disease allele is

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31. If a mother carries an X-linked disorder, meaning that she has one normal X chromosome and one mutated X chromosome, there is a 50 percent chance that a male fetus will have the disorder because males only have one X chromosome. *About X-Linked Disorders*, CENTERS FOR DISEASE CONTROL AND PREVENTION (Aug. 28, 2006), [http://www.cdc.gov/ncbddd/single\\_gene/x-link.htm](http://www.cdc.gov/ncbddd/single_gene/x-link.htm).

32. See Wright, *supra* note 7, at 22 (listing Acu-Gen Baby Gender Mentor, Pink And Blue Early DNA Gender Test, DNA Plus fetal test and paternity test).

33. Lo, *Non-invasive Prenatal Detection*, *supra* note 2, at 153.

34. Wright & Burton, *supra* note 4, at 143.

35. *Id.*

36. Huntington's disease is a genetic disease caused by a mutation on chromosome 4 that causes neurological degeneration. The typical age of onset is in the 30s or 40s and common symptoms include restlessness, facial movements, unsteady gait, quick sudden jerking movement of limbs, loss of memory, loss of judgment, personality changes and disorientation. *Huntington's Disease*, MEDLINEPLUS (June 24, 2009), <http://www.nlm.nih.gov/medlineplus/ency/article/000770.htm>.

37. Achondroplasia is a genetic disorder of bone growth that results in abnormal body proportions such as short arms and legs, with a relatively normal size torso. Children with achondroplasia are likely to have poor muscle-tone, leading to developmental delays in crawling, walking and other motor skills. *Achondroplasia*, MARCH OF DIMES (Sept. 2008), [http://www.marchofdimas.com/Baby/birthdefects\\_achondroplasia.html](http://www.marchofdimas.com/Baby/birthdefects_achondroplasia.html).

sufficient to inherit the disease, cffDNA testing can be diagnostic if the father, but not the mother, has the disease allele.<sup>38</sup> However, creating tests for autosomal recessive disorders, such as cystic fibrosis<sup>39</sup> and Tay Sachs,<sup>40</sup> in which the fetus must receive a disease allele from both the mother and father to inherit the disease, proved more challenging. Initially, cffDNA testing could be used to diagnose the fetus only if the mother had the recessive disease, because only the single recessive allele would be present in the maternal blood stream.<sup>41</sup> For the more common case, where the mother was a carrier, with one normal allele and one disease allele, cffDNA testing could not be used to diagnose the fetus.<sup>42</sup>

However, a new approach, known as digital relative mutation dosage (digital RMD), offers a possible method for geneticists to diagnose a fetus with an autosomal recessive disorder, even if its mother was a carrier.<sup>43</sup> Digital RMD first divides all cell free DNA in the maternal blood into groups of normal and disease alleles.<sup>44</sup> Geneticists then examine whether the amounts of normal and disease alleles in the maternal plasma sample are in allelic balance or imbalance.<sup>45</sup> If the ratio of normal and disease alleles is balanced, then geneticists expect the fetus to be a carrier of the disease, like its mother. If the alleles are imbalanced, the disease allele is either over- or underrepresented. Overrepresentation of the disease allele indicates the fetus has two copies of the disease allele and therefore will have the disease.<sup>46</sup> Alternatively, underrepresentation indicates that the fetus has two copies of

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38. Lun, *supra* note 13, at 19920.

39. Cystic fibrosis is a genetic disease of the mucus glands that affects numerous systems in the body. Symptoms of the disorder include progressive deterioration of the respiratory system and chronic digestive problems. *Cystic Fibrosis*, GENETICS HOME REFERENCE (Jan. 2008), <http://ghr.nlm.nih.gov/condition/cystic-fibrosis>.

40. Tay Sachs is a rare genetic disorder that causes progressive destruction of the nerve cells in the brain and spinal cord. As the disease progresses, children experience seizures, vision and hearing loss, intellectual disability and paralysis. *Tay Sachs Disease*, GENETICS HOME REFERENCE (Sept. 2008), <http://ghr.nlm.nih.gov/condition/tay-sachs-disease>.

41. Caroline Wright, *Advances in Non-Invasive Prenatal Diagnosis of Recessive Diseases*, PHG FOUNDATION, available at <http://www.phgfoundation.org/news/4422/>.

42. Lun, *supra* note 13, at 19920. The mother's blood will have high levels cffDNA with both the wild-type and mutated allele because the mother carries both alleles. Originally, researchers could not distinguish which alleles came from the fetus and which ones came from the mother, unless the fetus carried a paternally derived mutation.

43. *Id.* at 19921.

44. *Id.*

45. *Id.*

46. *Id.*

the normal allele and will not have the disease nor be a carrier.<sup>47</sup> Scientists have recently furthered this method by using known maternal haplotypes (based on nearby SNP alleles on the same chromosome) to analyze the relative haplotype dosage to provide significantly more information on the fetal genome.<sup>48</sup> At high enough throughput volume, comparing overall ratios of cell free DNA in maternal blood with certain characteristics offers a promising avenue for developing diagnostic reproductive genetic tests using cffDNA.

#### 4. Chromosomal Abnormalities

While identifying variations between maternal and fetal DNA has proven effective for detecting conditions associated with a single gene, using these variations to diagnose diseases associated with an entire chromosome, such as Down syndrome,<sup>49</sup> has been challenging.<sup>50</sup> However, researchers have successfully created testing protocols that examine very small differences in the ratios of the amount of cffDNA from each chromosome present in maternal blood serum. Dennis Lo and colleagues isolated and amplified DNA regions on the chromosomes of interest and then compared the overall dosage of the chromosome of interest to the dosage of a reference

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47. *Id.*

48. Lo et al., *supra* note 3, at 4.

49. Down syndrome results from having an extra copy of the 21st chromosome. Common symptoms of Down syndrome include intellectual impairment, severe learning disabilities, and shortened lifespan resulting from long term health problems, such as heart disease. The incidence of Down syndrome increases with maternal age from about .07 percent at age twenty to 1 percent at age forty. *See Down syndrome*, US NAT'L LIBRARY HEALTH, (Oct. 18, 2010), <http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001992/>; *see also Down syndrome*, NAT'L INST. OF HEALTH (Feb. 17, 2012), [http://www.nichd.nih.gov/health/topics/down\\_syndrome.cfm](http://www.nichd.nih.gov/health/topics/down_syndrome.cfm).

50. Fan & Quake, *supra* note 5, at 1. Researchers have struggled to detect aneuploidies (abnormal numbers of chromosomes) using cffDNA in maternal blood plasma because they must selectively target a number of fetal DNA sequences on specific chromosomes and then find differences in the ratio of genetic markers for each chromosome, rather than simply differences in the DNA sequence between the mother and fetus. Fan & Quake, *supra* note 5, at 1; Lo, *Non-invasive Prenatal Detection*, *supra* note 2, at 153 (discussing methods to do so using placental mRNA, epigenetic markers, and digital PCR). *See also*, Y.M. Dennis Lo et al., *Plasma Placental RNA Allelic Ratio Permits Non-invasive Prenatal Chromosomal Aneuploidy Detection*, 13 NATURE MEDICINE 218 (2007); Ravinder Dhallan et al., *A Non-invasive Test for Prenatal Diagnosis Based on Fetal DNA Present in Maternal Blood: A Preliminary Study*, 369 LANCET 474 (2007).

chromosome.<sup>51</sup> As with genetic alleles, even small increases or decreases in the expected dosage of a particular chromosome can indicate aneuploidy, an abnormal number of chromosomes, in the fetus. Steve Quake and colleagues from Stanford University quantified the number of DNA sequences that came from each chromosome and then analyzed the results for over- and underrepresentation of a particular chromosome in the fetus.<sup>52</sup> Both studies demonstrated a high level of accuracy in detecting Down syndrome, in which a fetus has three copies of the twenty-first chromosome.<sup>53</sup>

Initially, NIPD testing for Down syndrome will be used to rule out Down syndrome in pregnancies that have screened high risk for the disorder, thereby greatly limiting the number of women that would require invasive prenatal diagnosis (IPD) in the form of an amniocentesis or CVS.<sup>54</sup> Current screening techniques have false positive rates of about 5 percent, and all of those women are offered IPD. NIPD can rule out Down syndrome in 98 percent of those cases, meaning that only 0.1 percent of all pregnant women would need a referral for IPD to detect Down syndrome.<sup>55</sup> As the cost of NIPD decreases, researchers anticipate that it could become the first tier screen offered to all women for Down syndrome and other chromosomal abnormalities.<sup>56</sup>

## 5. Whole Genome Sequencing

Lo and Quake have now moved beyond single gene testing and chromosomal analysis to whole genome sequencing of the fetus from a maternal blood sample. In a proof-of-principle paper published December 8, 2010, Dennis Lo and colleagues mapped an entire fetal genome from cfDNA present in maternal blood plasma.<sup>57</sup> They also demonstrated that

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51. Y.M. Dennis Lo et al., *Digital PCR for the Molecular Detection of Fetal Chromosomal Aneuploidy*, 104 PROC. NATL. ACAD. SCI. 13116, 13117 (2007). Lo and colleagues used digital PCR to isolate and amplify the DNA sequences of interest.

52. Fan & Quake, *supra* note 5, at 1. Quake used simultaneous shotgun sequencing, a method for sequencing long strands of DNA. It gets its name from the similarity between the method and the rapidly-expanding, quasi-random firing pattern of a shotgun.

53. *Id.* at 2; see also Rossa W.K. Chiu et al., *Non-Invasive Prenatal Assessment of Trisomy 21 by Multiplexed Maternal Plasma DNA Sequencing: Large Scale Validity Study*, 342 BRIT. MED. J. 7401, 7407 (2011), available at <http://www.bmj.com/content/342/bmj.c740>. This study also revealed a high level of accuracy at detecting other forms of aneuploidy, including Trisomy 18 (Edward Syndrome) and Trisomy 13 (T13).

54. Chiu et al., *supra* note 53, at 7–8.

55. *Id.*

56. *Id.*

57. Lo et al., *supra* note 3, at 9.

cffDNA from all regions of the fetal genome was present in the maternal blood in a constant relative proportion to maternal cell-free DNA.<sup>58</sup> Stephen Quake and colleagues used data known about the parents' DNA and the relative frequency of those sequences in the cell free DNA blood sample to help identify which DNA sequences were inherited from each parent, and therefore the genotype of the fetus.<sup>59</sup> These discoveries mean that the entire fetal genome could be analyzed from a non-invasive blood test and the genotype of the parents.<sup>60</sup> Such a test could offer prospective parents information on inherited genetic conditions as well as spontaneous mutations in the fetal genome.<sup>61</sup> Lo stated that the only limitations on this form of fetal genetic analysis are the depth of sequencing available and the resolution of the parental genetic maps.<sup>62</sup> Over time, sequencing technology should improve and the cost should continue to drop, easing access to whole genome sequencing for both parental and fetal genomes.<sup>63</sup> Before genome-wide analysis becomes available, Lo and colleagues suggest that this technology may be used for targeted sequencing approaches to test for multiple disease-related regions at one time, which would greatly reduce the cost of prenatal testing for multiple conditions.<sup>64</sup>

Currently, NIPD is only commercially available to test for Down syndrome, Trisomy 13, Trisomy 18, RhD status and fetal sex.<sup>65</sup> The availability of NIPD testing for a variety of known genetic diseases, conditions and predispositions is likely to slowly accelerate over the next decade.<sup>66</sup> Beyond diseases caused by chromosomal abnormality, fetal sex

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58. *Id.*

59. Fan & Quake, *supra* note 5.

60. *Id.*; see also Lo et al., *supra* note 3, at 9.

61. Fan & Quake, *supra* note 5.

62. *Id.*

63. *Id.*

64. Lo et al., *supra* note 3, at 10.

65. Lauren C. Sayres & Mildred K. Cho, *Cell-Free Fetal Nucleic Acid Testing: A Review of the Technology and its Applications*, OBSTETRICAL AND GYNECOLOGICAL SURVEY 7-9 (accepted for publication 2011 and on file with author). See generally, *DNA Fetal Gender Determination*, CTR. FOR MED. GENETICS, <http://www.geneticstesting.com/gendertest/gendertest.htm> (last visited March 16, 2012); *Fetal cell/DNA Prenatal Gender Test*, DNAPLUS.COM, [http://www.dnaplus.com/fetal\\_cell\\_prenatal\\_geder\\_test.htm](http://www.dnaplus.com/fetal_cell_prenatal_geder_test.htm), (last visited March 16, 2012); *Early DNA Gender Predicting Test: Boy or Girl?*, TELLMEPINKORBLUE.COM, <http://www.tellmepinkorblue.com/Gender-Testing-Boy-Girl.php> (last visited March 16, 2012); *Prenatal Gender Testing on Maternal Blood: Y-Chromosome Detection*, PRENATAL GENETICS CTR., <http://www.prenatalgeneticscenter.com/gender-intro.asp> (last visited March 16, 2012); Wright, *supra* note 7; SEQUENOM, *supra* note 4.

66. Wright & Chitty, *supra* note 10, at 164.

and Mendelian genetic diseases, NIPD may one day also be able to offer parents full analysis of their fetus' entire genome.<sup>67</sup>

*B. Is There Anything New Here?*

The fact that NIPD offers a new form of prenatal genetic testing does not guarantee a revolution in reproductive practices. Reproductive fetal genetic testing has been possible for over forty years,<sup>68</sup> but has not yet penetrated into the core of society as deeply as predicted in Aldous Huxley's *Brave New World* or the 1990s science fiction film, *Gattaca*.<sup>69</sup> In fact, in 2009, physicians in the United States performed IPD on less than 2 percent of all pregnancies.<sup>70</sup> However, three features of cffDNA testing distinguish it from current forms of reproductive genetic testing in ways that are critical. First, the testing is non-invasive. Second, it is offered early in the pregnancy, and third, it will be less expensive. As a result, cffDNA testing has the potential to eliminate many of the existing obstacles to diagnostic reproductive genetic testing and in doing so dramatically expand the volume of pregnant women receiving prenatal diagnosis and increase the scope of genetic information for which they are willing to test. And that would be revolutionary.

1. Current Prenatal Genetic Testing

The benefits of cffDNA testing are best understood in comparison to current prenatal and preimplantation genetic testing techniques. Currently, pregnant women take very different paths with respect to prenatal genetic testing. Some women know that they do not wish to receive any genetic information about their fetus, therefore they will decline both prenatal genetic screening, which will provide them with probabilistic information (e.g., 1 in 200 or 1 in 5) on whether their child will have a specific genetic disorder, and invasive prenatal diagnosis, which will provide them with diagnostic information on whether their child has the disorder (e.g., positive or negative). Other women know that they definitely want diagnostic information as early as possible and are willing to undergo an invasive test

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67. Lo et al., *supra* note 3, at 9.

68. Joseph Woo, A SHORT HISTORY OF AMNIOCENTESIS, FETOSCOPY, AND CHORIONIC VILLUS SAMPLING, <http://www.ob-ultrasound.net/amniocentesis.html>.

69. See ALDOUS HUXLEY, *BRAVE NEW WORLD* (Harper & Brothers 1932); *GATTACA* (Columbia Pictures Corp. 1997).

70. Henry T. Greely, *Get Ready for the Flood of Fetal Genetic Screening*, 469 NATURE 289, 289 (2011).

with a slight risk of miscarriage to receive it. Frequently, these women either have a family history of a genetic disorder or they are at advanced maternal age (over thirty-five), which increases the risk of Down syndrome and other disorders. Such women commonly receive IPD in the form of chorionic villus sampling (CVS) between ten and fourteen weeks gestation.<sup>71</sup> In general, women with strong opinions either against screening or for immediate invasive diagnostic testing tend to be in the minority.

Most pregnant women elect to have prenatal genetic screening to determine whether their fetus is at elevated risk for a specific disorder, and then, if so, make a decision regarding diagnostic prenatal testing.<sup>72</sup> Prenatal genetic screening can include anything from a single blood test in the second trimester (fifteen to twenty weeks) to a series of tests—a blood test between ten and thirteen weeks, an ultrasound between eleven and thirteen weeks, and another blood test between fifteen and twenty weeks.<sup>73</sup> The more information gathered during the screening process, the more accurate the screening results. Currently, prenatal genetic screening offers prospective parents risk information for open neural tube defects, abdominal wall defects, certain genetic diseases, such as Smith-Lemli-Optiz syndrome, and chromosomal abnormalities, such as Down syndrome.<sup>74</sup> Both the blood tests and the ultrasound have limitations. The blood tests only provide information on the probability that the fetus will be affected based on certain markers in the blood, which can often be difficult to interpret for parents and providers, and ultrasound only detects physical anomalies.<sup>75</sup> If the fetus screens positive for any of these conditions, the pregnant woman must decide whether to wait until the fetus is born to know if it has a disorder, or undergo another form of IPD, known as amniocentesis,<sup>76</sup> to provide diagnostic information about the

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71. THE CALIFORNIA PRENATAL SCREENING PROGRAM, RESULTS FOR SCREENING IN THE FIRST TRIMESTER—THE RESULT OF YOUR SCREENING TEST IS: SCREEN POSITIVE FOR DOWN SYNDROME 5 (California Department of Public Health ed., 2009). CVS is an invasive procedure that uses a needle or a tube inserted through the cervix to remove fetal cells from the placenta for genetic testing.

72. Laura L. Jelliffe-Pawlowski et al., *Using Second Trimester Ultrasound and Maternal Serum Biomarker Data to Help Detect Congenital Heart Defects in Pregnancies with Positive Triple-marker Screening Results*, 146 AM. J. HUM. GENETICS 2455, 2456 (2008).

73. Prenatal Screening Program, CALIF. DEPARTMENT OF PUBLIC HEALTH (2010), <http://www.cdph.ca.gov/programs/pns/Pages/default.aspx>.

74. *Id.*

75. Ainsley J. Newson, *Ethical Aspects Arising from Non-Invasive Fetal Diagnosis*, 13 SEMINARS IN FETAL & NEONATAL MED. 103, 103 (2008).

76. THE CALIFORNIA PRENATAL SCREENING PROGRAM, *supra* note 71, at 7. Amniocentesis involves collecting the fetal cells needed for testing by inserting a needle through the abdominal wall to remove a small amount of amniotic fluid surrounding the fetus.



fetus prior to birth.<sup>77</sup> Physicians can perform an amniocentesis during the second trimester between fifteen and twenty-four weeks gestation.<sup>78</sup>

Both forms of IPD, amniocentesis and CVS, cost around \$1,500, are uncomfortable for the woman, and have about a 0.5 to 1 percent risk of miscarriage.<sup>79</sup> As a result, most women currently do not opt for any form of diagnostic prenatal genetic testing unless a serious genetic or chromosomal disorder runs in their family or they screen high risk for a disease that would cause them to consider pregnancy termination.<sup>80</sup> In addition, these risks limit the conditions for which physicians will offer IPD, as ethically they must balance the risks of a procedure with its benefits.<sup>81</sup> Therefore with IPD, a physician should only offer testing when the informational benefit provided to the couple could outweigh the miscarriage risk and discomfort.<sup>82</sup> This limits both the number of women who undergo prenatal diagnostic testing and the conditions for which testing is available.

## 2. Preimplantation Genetic Diagnosis

Women can also receive reproductive genetic testing prior to pregnancy in the context of *in vitro* fertilization (IVF) accompanied by preimplantation

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77. *Id.* at 4–7.

78. *Id.* at 7.

79. Wright, *supra* note 7, at 11. The risk of miscarriage associated with CVS and amniocentesis varies by the skill of the provider, and can in some cases be much lower (1 in 200). See A.B. Caughey, L.M. Hopkins & M.E. Norton, *Chorionic Villus Sampling Compared with Amniocentesis and the Difference in the Rate of Pregnancy Loss*, 108 OBSTETRICS & GYNECOLOGY 612, 612–16 (2006) (performed over 20 years at UCSF and finding an overall miscarriage rate of 3.2% for CVS and .8% miscarriage rate for amniocentesis); A. Tabor, C.H.F. Vestergaard, & O. Lidegaard, *Fetal Loss Rate After Chorionic Villus Sampling and Amniocentesis: an 11-Year National Registry Study*, 34 ULTRASOUND OBSTETRICS & GYNECOLOGY 19, 19–24 (2009) (performed in Denmark, but demonstrating miscarriage rates of 1.4% for amniocentesis and 1.9% for CVS, and showing a significant reduction in miscarriage in clinics that performed more than 1500 CVS procedures a year). The price for amniocentesis and CVS vary by hospital and provider, however general estimates range from \$1100–\$2000. See e.g. KayCircle, *What is the Average Cost of Amniocentesis?* available at: <http://www.kaycircle.com/What-is-the-average-cost-of-an-Amniocentesis-without-health-insurance-Amniotic-fluid-test-AFT-Price-Range>.

80. See Anita de Jong et al., *Non-invasive Prenatal Testing: Ethical Issues Explored*, 18 EUR. J. HUM. GENETICS 272, 273 (2010).

81. Greely, *supra* note 70, at 289; Dagmar Schmitz et al., *No Risk, No Objections? Ethical Pitfalls of Cell-free Fetal DNA and RNA Testing*, 339 BRIT. MED. J. 165, 165 (2009).

82. While the informational value to the couple is not for the physician to decide in a particular case, the physician should not offer testing for those conditions where the benefit could not outweigh the clinical risk.

genetic diagnosis (PGD).<sup>83</sup> PGD permits prospective parents to make reproductive decisions prior to implantation of an embryo, which enables them to avoid a termination decision based on the genetic and chromosomal status of their fetus.<sup>84</sup> To perform IVF, a clinician harvests eggs from the woman and combines each egg with sperm in a Petri dish in hopes of fertilization.<sup>85</sup> On the third day after fertilization, an embryologist removes one cell from each embryo that has fertilized and developed to an eight-cell stage, and then sends the DNA inside that cell to a laboratory for genetic testing.<sup>86</sup> The prospective parents can then decide which embryos to transfer to the womb based on the results of the test.<sup>87</sup>

PGD has a number of drawbacks that limit its use in the United States to a few thousand cycles per year.<sup>88</sup> First and foremost, this method of reproductive genetic testing is significantly more expensive than prenatal testing, costing around \$10,000 to \$12,000 per IVF cycle and an additional \$6,500 to \$8,500 for PGD.<sup>89</sup> The sheer cost alone is sufficient to make PGD financially inaccessible for many couples. Second, the procedure carries risks to both the woman undergoing the procedure and the fetus.<sup>90</sup> In order to retrieve the eggs for fertilization, the woman must take large doses of hormones to trigger her ovaries to release more than one egg, be put under anesthesia, and have minor surgery.<sup>91</sup> Children born through IVF also experience slightly higher rates of congenital malformations and birth defects.<sup>92</sup> Finally, in addition to the expense and the risk, each IVF and PGD

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83. *Preimplantation Genetic Diagnosis (PGD)*, IVF-INFERTILITY.COM (June 19, 2011), <http://www.ivf-infertility.com/ivf/pgd.php>.

84. *Id.*

85. *Id.*

86. *Id.*

87. *Id.*

88. Jaime S. King, *Predicting Probability: Regulating the Future of Preimplantation Genetic Screening*, 8 YALE J. HEALTH POL'Y L. & ETHICS 283, 291 n.28 (2008). The number of PGD cycles that occur each year is difficult to calculate as this data is not collected by any entity, including the CDC as part of its ART database. The most recent data from 57 clinics in Europe found that 5887 cycles were completed in 2007, resulting in 1206 babies born. J.C. Harper et al., *ESHERE PGD Consortium Data Collection X: Cycles from January to December 2007, with Pregnancy Follow-up to October 2008*, 25 HUM. REPRODUCTION 2685, 2685 (2010).

89. See, e.g., *In Vitro Fertilization*, NOVAIVF.COM, <http://novaivf.com/cost-ivf-pgd.htm> (last visited Aug. 3, 2011).

90. King, *supra* note 88, at 303–08.

91. *Id.* at 308.

92. *Id.* at 303–08.

cycle only has about a 30 percent chance of producing a viable pregnancy, which may cause many prospective parents to opt against the procedure.<sup>93</sup>

### 3. NIPD through CffDNA Testing

While prenatal and preimplantation diagnostic testing can provide parents with the ability to engage in reproductive selection for a wide variety of conditions, due to the risks and expense of the procedures, prospective parents use these methods only in rare instances.<sup>94</sup> By comparison, cffDNA testing has three critical features that differentiate it from current methods of reproductive genetic testing in ways that will remove many of the existing roadblocks for prenatal genetic testing. It offers diagnostic information from a non-invasive test that is available early in pregnancy, and will be comparatively less expensive.

First, the cffDNA testing can be completed from a maternal blood test, making it non-invasive of the uterus.<sup>95</sup> Therefore, it eliminates any risk to the fetus and reduces discomfort to the mother, which may significantly alter pregnant women's opinions regarding testing.<sup>96</sup> Currently, less than 2 percent of all pregnant women receive diagnostic prenatal or preimplantation genetic testing due to the expense, discomfort, and risks to mother and fetus.<sup>97</sup> However, in California, where all pregnant women are required by law to be offered prenatal screening, which offers only probabilistic information, approximately 70 percent accept.<sup>98</sup> This demonstrates that a substantial majority of pregnant women may have both an interest in genetic information about their fetus and a willingness to undergo a blood test to gain that information. A woman who was willing to have a blood test to obtain probabilistic genetic risk information is likely to be equally willing to

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93. CENTERS FOR DISEASE CONTROL AND PREVENTION, AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE, & SOCIETY FOR ASSISTED REPRODUCTIVE TECHNOLOGY, 2008 ASSISTED REPRODUCTIVE TECHNOLOGY SUCCESS RATES: NATIONAL SUMMARY AND FERTILITY CLINIC REPORTS 22 (U.S. Department of Health and Human Services 2010), available at [http://www.cdc.gov/art/ART2008/PDF/ART\\_2008\\_Full.pdf](http://www.cdc.gov/art/ART2008/PDF/ART_2008_Full.pdf) (last visited Aug. 3, 2011).

94. Peter Benn & Audrey Chapman, *Practical and Ethical Considerations of Noninvasive Prenatal Diagnosis*, 301 JAMA 2154, 2154 (2009).

95. *Id.* While NIPD is generally referred to as being non-invasive, it does require a needle stick for the blood draw.

96. Benn & Chapman, *supra* note 94, at 2155.

97. See Greely, *supra* note 70, at 289.

98. Jelliffe-Pawlowski et al., *supra* note 72, at 2456. California offers prenatal genetic screening to all pregnant women. As a result, the uptake of prenatal screening is likely to be higher than the rest of the country. However, this finding does suggest a desire among women to have such information. See *id.*

have a similar blood test that would provide her with significantly more accurate or diagnostic information.<sup>99</sup>

At initial obstetrics appointments, most pregnant women already undergo a number of blood tests, which should ease the integration of NIPD into early prenatal care for both physicians and patients.<sup>100</sup> Physicians would need to add an additional lab test to their standard list, and patients must be willing to have an additional vial of blood drawn. As a result of the ease of integrating the testing procedure, pregnant women are more likely to have the test and view it as part of standard prenatal care. One expectant mother stated upon being told about NIPD, "If I had the opportunity to take a blood test instead of amniocentesis, I would take the blood test hands down . . . You get poked a million times anyway when you are pregnant. Another blood test is no big deal. But a needle going in the amniotic sac and potentially harming the baby is scary, particularly at an older age."<sup>101</sup> As a result, more women may decide to have the test, and more physicians may offer it for a wider range of conditions.

Second, NIPD can be given to women very early in the pregnancy, in some cases as early as seven to nine weeks gestation.<sup>102</sup> This offers

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99. In fact, women may be more willing to have a non-invasive diagnostic test than a non-invasive screening test, due to the need to verify a positive screening test with an invasive procedure, such as an amniocentesis or CVS. Initially, many obstetricians may advise patients to follow any NIPD testing results with IPD to verify results. However, if NIPD methods prove as accurate as the early clinical trials suggest, it seems likely that it will replace IPD altogether. See Loes Kooij et al., *The Attitude of Women Toward Current and Future Possibilities of Diagnostic Testing in Maternal Blood Using Fetal DNA*, 29 *PRENATAL DIAGNOSIS* 164, 166 (2009) (81 percent of pregnant women felt that NIPD should be offered to all pregnant women to diagnose Down syndrome, while only 74 percent felt that all pregnant women should be offered prenatal genetic screening for Down syndrome).

100. See *Routine Tests in Pregnancy*, AM. COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS, [http://www.acog.org/publications/patient\\_education/bp133.cfm](http://www.acog.org/publications/patient_education/bp133.cfm) (last visited Feb. 21, 2011); William Sears & Martha Sears, *Prenatal Checkups: Month by Month What to Expect When Seeing Your Doctor*, ASKDRSEARS.COM, <http://www.askdrsears.com/html/1/t011200.asp> (last visited Feb. 21, 2011), Mayo Clinic Staff, *Prenatal Care First Trimester Visits*, MAYOCLINIC.COM, <http://www.mayoclinic.com/health/prenatal-care/PR00008> (last visited Feb. 1, 2011).

101. *New Down syndrome Test Could Cut Healthy Baby Deaths, Non-Invasive Blood Test Could Eliminate Miscarriage Risk of Amniocentesis*, ABCNEWS.GO.COM, <http://abcnews.go.com/Health/prenatal-test-down-syndrome-cut-baby-deaths-amniocentesis/story?id=12594077&page=2> (last visited Feb. 21, 2011).

102. Alison Hall et al., *Non-Invasive Prenatal Diagnosis Using Cell-Free Fetal DNA Technology: Applications and Implications*, 13 *PUB. HEALTH GENOMICS* 246, 248 (2010). Seven weeks gestation means seven weeks from the first day of the woman's last menstrual period. By this measure, a woman would miss her period at four to five weeks gestation.

significant benefits for decision-making and clinical care. In comparison, the earliest CVS and amniocentesis can be offered is ten and fifteen weeks, respectively.<sup>103</sup> However, most women will not receive diagnostic information until later in their second trimester, because most of them only opt for amniocentesis following a positive prenatal screening result.<sup>104</sup> As noted above, prenatal screening protocols cannot be completed prior to fifteen weeks, and then a pregnant woman must wait for the results. If her pregnancy screens “high risk,” and she wants to consider IPD, then she must make an appointment with her obstetrician and/or genetic counselor to determine whether to undergo an amniocentesis. If she opts to have the IPD, she must schedule an appointment, have the procedure and again await the results. All of this can take a few weeks, meaning that if her fetus tests positive for a disorder, she will likely decide whether to terminate the pregnancy closer to eighteen to twenty weeks. Many states prohibit pregnancy terminations beyond twenty-four weeks gestation except to save the life of the mother, which greatly limits the amount of time prospective parents have to think about their decision and the options available with respect to termination.<sup>105</sup>

In addition, possessing diagnostic information early in the first trimester provides significant clinical benefits. In some cases, early detection can improve clinical decision-making by permitting prenatal treatment to alleviate symptoms of a disorder or improve the clinical management of the pregnancy or birth.<sup>106</sup> For instance, administering antenatal dexamethasone to female fetuses affected by congenital adrenal hyperplasia at or before ten weeks gestation can reduce genital ambiguity.<sup>107</sup> Also, as noted above, testing levels of cfDNA in maternal blood can identify abnormal placental function before significant symptoms arise allowing for improved

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American Pregnancy Association, *Calculating Your Dates: Gestation, Conception and Due Date*, available at <http://www.americanpregnancy.org/duringpregnancy/calculatingdates.html>. Currently, aneuploidy testing is offered at nine weeks, but given the presence of cfDNA in maternal blood earlier in the pregnancy, companies are likely to move this date forward.

103. THE CALIFORNIA PRENATAL SCREENING PROGRAM, *supra* note 71.

104. See Naomi Nakata, Yuemei Wang & Sucheta Bhatt, *Trends in Prenatal Screening and Diagnostic Testing Among Women Referred for Advanced Maternal Age*, 30 *Prenatal Diagnosis* 198, 198–206 (2010).

105. See AUBREY MILUNSKY & JEFF MILUNSKY, *GENETIC DISORDERS AND THE FETUS: DIAGNOSIS, PREVENTION AND TREATMENT* 940 (6th ed. 2010).

106. See Hall et al., *supra* note 102, at 248–49.

107. *Id.*; see generally Robert J. P. Rijnders et al. *Clinical Applications of Cell-free Fetal DNA from Maternal Plasma*, 103 *OBSTETRICS & GYNECOLOGY* 157, 157–64 (2004).

monitoring and prenatal care from an earlier point in the pregnancy.<sup>108</sup> The earlier timing of NIPD offers significant benefits both clinically and for patients' decision-making processes. The significance of this timing shift will be further discussed in more detail in Part IIIC.

Third, NIPD will be less expensive than current forms of prenatal or preimplantation genetic testing, making it more easily accessible. The cost of DNA sequencing is rapidly dropping.<sup>109</sup> In 2008, Steve Quake estimated the cost of his aneuploidy test would be approximately \$700.<sup>110</sup> By 2010, the price had dropped nearly 60 percent to \$300.<sup>111</sup> As DNA sequencing technology improves, the cost of genetic testing is expected to continue to drop, so much so that the cost of sequencing of an entire human genome has been estimated to be under \$1,000 within two years.<sup>112</sup> While the reduction in cost will lower the expense of all prenatal and preimplantation genetic testing, the costs of IPD and PGD will remain much higher due to the clinical expertise and setting required to perform the procedure. As a result, NIPD will offer newly pregnant women a less risky, comparably inexpensive way to find out a great deal about their fetus' genetic makeup almost immediately upon discovering they are pregnant.

## II. THE DIFFERENCE cffDNA MAKES

This combination of factors raises the importance of considering the implications of widespread reproductive genetic testing from an interesting thought exercise to an imperative social concern. It does so by increasing the number of women who will undergo reproductive genetic testing, broadening the scope of conditions and characteristics that can be tested for, and providing genetic information to parents at a point in the pregnancy when the information is more actionable.

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108. See Wright & Burton, *supra* note 4, at 145; Hahn, et al, *supra* note 23.

109. Colin Hill, *Beyond the \$1000 Genome*, FORBES, available at <http://www.forbes.com/sites/colinhill/2012/02/09/beyond-the-1000-genome/>.

110. Steven R. Quake, Lecture, *Implications of Maternal Serum Fetal Cell Free DNA Conference*, STANFORD LAW SCHOOL (May 7, 2010), [http://www.law.stanford.edu/display/images/dynamic/events\\_media/20100507\\_CLB\\_MaternalSerum-001.mov](http://www.law.stanford.edu/display/images/dynamic/events_media/20100507_CLB_MaternalSerum-001.mov).

111. *Id.*

112. Rachel Lehmann-Haupt, *Pacific BioScience Has a \$1000 Genome Test That Could Save Your Life – And The Industry*, BNET HEALTHCARE (March 4, 2010), <http://www.bnet.com/blog/healthcare/pacific-bioscience-has-a-1000-genome-test-that-could-save-your-life-and-the-industry/1824>. While this timeline may be ambitious, it nonetheless demonstrates the rapid decrease in high throughout genetic screening.

*A. Increase in Volume*

Due to the clinical advantages of NIPD over existing reproductive genetic testing techniques, its adoption into clinical practice will expand the number of pregnant women who receive prenatal genetic testing. The scope of the increase will depend on three major factors: 1) the underlying patient demand for fetal genetic information; 2) the rate of adoption of NIPD testing by OB/Gyns; and 3) the level of insurance coverage for the procedure. Importantly, these three factors are not independent of one another, such that as patient demand and physician support increases, so will the likelihood of insurance coverage. The inverse is also true, as insurance coverage expands patient demand and physician adoption will also increase.

Patient demand for fetal genetic information depends on the ease of obtaining the information and its quality. Pregnant women will be more likely to undergo reproductive genetic testing as expense, discomfort and risk decrease and the quantity and quality of genetic information available increase.<sup>113</sup> NIPD offers an improvement over current reproductive genetic testing technologies at each of these levels. As mentioned above, the reduction in risk and discomfort associated with NIPD will likely cause many women to recalculate their decision to have prenatal screening and testing. One group of pregnant women, surveyed in the Netherlands, strongly supported the use of NIPD on a societal level for health-related conditions.<sup>114</sup> The study found that 81 percent of pregnant women agreed that NIPD should be offered to all pregnant women to diagnose Down syndrome, while only 45 percent agreed that invasive diagnostic tests should be offered to all woman to diagnose Down syndrome.<sup>115</sup> While the attitudes of pregnant women in the U.S. may differ somewhat from pregnant women in the Netherlands, the demand for fetal genetic information obtained in a non-invasive manner is likely to be quite high.<sup>116</sup> Further, as with all genetic testing, the cost of NIPD should continue to decrease, while the range of conditions available for testing and the reliability of information should increase.<sup>117</sup>

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113. Benn & Chapman, *supra* note 94, at 2154.

114. Kooij, *supra* note 99, at 166.

115. *Id.* Interestingly, a comparison group of female medical students felt strongly that NIPD is "an important asset in screening for Down syndrome" (89 percent), but only about half felt that it should be offered to all pregnant women to test for Down syndrome (49 percent). *Id.*

116. Benn & Chapman, *supra* note 94, at 2154.

117. Greely, *supra* note 70, at 290.

Similarly to patients, physicians will adopt a new technology when the balance of its advantages and disadvantages offer an improvement over a similar comparison for the existing technology.<sup>118</sup> For instance, if a new medical device offers greater clinical advantages with fewer disadvantages for a similar price, the device will likely be widely adopted. With NIPD, the clinical advantages of diagnostic genetic information at an earlier point in the pregnancy accompanied by an substantial decrease in risk and cost when compared to current prenatal and preimplantation genetic diagnosis make the case for its adoption quite compelling.<sup>119</sup>

The potential for a wrongful birth lawsuit may also speed the integration of NIPD into standard prenatal care. Wrongful birth suits permit prospective parents to sue a physician for negligence in testing or failing to offer genetic tests, that if given, would have identified a genetic disorder in the fetus and permitted the prospective parents to abort the fetus.<sup>120</sup> Wrongful birth suits do not permit the prospective parents to recover for the genetic disorder itself, but rather for the loss of the choice to terminate the pregnancy and the damages that result from that loss.<sup>121</sup> Physicians have argued in wrongful birth lawsuits that the risk of miscarriage associated with IPD justified not offering diagnostic testing to the patient. Given the reduced risk of fetal miscarriage associated with NIPD, physicians may feel obligated to offer prospective parents NIPD for a wide range of genetic disorders and conditions not currently part of the prenatal screening protocol to avoid a potential suit for wrongful birth.

As mentioned above, the speed of NIPD adoption will also largely depend on whether insurance companies cover its use. Insurance coverage will increase patient demand for the test and ease physician adoption. In the United States, both private and public health insurance offer coverage for prenatal care.<sup>122</sup> Private health plans are becoming more reluctant to offer coverage for new technologies in the absence of clinical research

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118. José J. Escarce, *Externalities in Hospitals and Physician Adoption of a New Surgical Technology: An Exploratory Analysis*, 15 J. HEALTH ECON. 715, 719 (1996).

119. Hall et al., *supra* note 102, at 248–49; *see also* Mary Norton, Professor of Obstetrics & Gynecology, Stanford Medical School, *Free Fetal DNA: The Provider and Patient Prospective*, Lecture at the Stanford University Implications of Maternal Serum Fetal Cell Free DNA Conference (May 7, 2010).

120. *See e.g.*, *Lininger v. Eisenbaum*, 764 P.2d 1202, 1212 (Colo. 1988); *Berman v. Allan*, 404 A.2d 8, 15 (Pa. 1979); *Becker v. Schwartz*, 386 N.E.2d 807, 819 (N.Y. 1978).

121. DAN B. DOBBS, *THE LAW OF TORTS* §291, at 793 (West 2000).

122. KAISER FAMILY FOUNDATION, *STATE MEDICAID COVERAGE OF PERINATAL SERVICES: SUMMARY OF STATE FINDINGS NOVEMBER 2009* 10 (2009), *available at* [www.kff.org/womenshealth/upload/8014.pdf](http://www.kff.org/womenshealth/upload/8014.pdf).



demonstrating its effectiveness overall, and its cost-effectiveness over existing technologies.<sup>123</sup> Private insurance companies are unlikely to cover NIPD without a rigorous testing period, but given NIPD's advantages over existing prenatal testing, eventual coverage of NIPD testing seems likely. This is especially true as each additional genetic disorder detected presents the possibility that the parents will abort the fetus, which, if born, could prove very costly for the insurance company.<sup>124</sup>

Given this potential insurance company viewpoint, it is essential to ensure that NIPD is presented in a way that enhances the ability of pregnant women to make an informed decision based on sound information and a clear assessment of her personal values, rather than simply promoting testing and abortion. Unfortunately, private insurance companies often reimburse for diagnostic tests at significantly higher levels than for pretest counseling.<sup>125</sup> Such a reimbursement model might lead physicians to spend their very small amount of compensated time encouraging NIPD, rather than helping patients determine which NIPD tests, if any, they desired.<sup>126</sup> If patients believe that NIPD testing for a wide range of conditions is an expected and accepted part of "good prenatal care", rather than an option to receive information that may assist in their reproductive decisions, many women may receive unexpected and unwanted information.<sup>127</sup> Such a result could be extremely detrimental for pregnant women seeking NIPD and should be avoided.

Obtaining public health insurance coverage through Medicaid will present additional challenges.<sup>128</sup> In the last two decades, Medicaid has

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123. Wade Aubrey, Professor of Medicine at UC San Francisco, Lecture at the Stanford University Implications of Maternal Serum Fetal Cell Free DNA Conference (May 7, 2010).

124. Carolyn Jacobs Chachkin, *What Potent Blood: Non-Invasive Prenatal Genetic Diagnosis and the Transformation of Modern Prenatal Care*, 33 AM. J. L. MED. 9, 40-43 (2007) (providing a detailed cost analysis of the financial benefits of covering NIPD for insurance companies); see also LORI HAMMON, THE COUNCIL FOR RESPONSIBLE GENETICS, NON-INVASIVE PRENATAL DIAGNOSIS 24 (2011).

125. Sonia Mateau Suter, *The Routinization of Prenatal Testing*, 28 AM. J. L. & MED. 233, 246 (2002).

126. *Id.*

127. The idea that unwanted and unexpected genetic information can be toxic for pregnant women is discussed further in Part IIIB.

128. THE KAISER COMMISSION ON MEDICAID AND THE UNINSURED & GEORGETOWN UNIVERSITY HEALTH POLICY INSTITUTE CENTER FOR CHILDREN AND THE FAMILY, NEW FEDERAL FUNDING AVAILABLE TO COVER IMMIGRANT CHILDREN AND PREGNANT WOMEN (July 2009), available at <http://www.kff.org/medicaid/7915.cfm>. The Children's Health Insurance Plan (CHIP) also can be used to cover prenatal care for pregnant women through the "unborn child" option, which provides for care to the fetus via the pregnant woman. *Id.* Overall this

become the single largest payer of maternity related services in the United States, financing four in ten of all births annually.<sup>129</sup> Medicaid currently covers the poor, aged, disabled, blind, and their dependent children; states can also extend coverage to low-income pregnant women and children.<sup>130</sup> In keeping with the recommendations of the American College of Obstetrics and Gynecology (ACOG) that all pregnant women should be offered prenatal genetic screening and/or diagnosis, in a survey of forty-four Medicaid programs, thirty-six states and the District of Columbia (D.C.) reported currently covering prenatal genetic screening services.<sup>131</sup> In addition, of the forty-four Medicaid programs, forty states and D.C. cover prenatal genetic diagnosis through CVS and forty-two states and D.C. cover it through amniocentesis.<sup>132</sup> Twenty-three state Medicaid programs and the D.C. Medicaid program also cover genetic counseling services for pregnant women.<sup>133</sup> In those states that have already adopted prenatal genetic screening, testing and counseling, coverage of a less expensive, non-invasive genetic testing option should be perfunctory, provided the accuracy and reliability of the test were similar.<sup>134</sup>

For those state Medicaid programs and private insurance plans that do not currently cover prenatal genetic testing and screening, the benefits of NIPD may shift the balance in favor of coverage. Since the children subsequently born will be covered either by the Medicaid or the parents' private insurance plan, engaging in early diagnosis through NIPD and prenatal treatment for placental complications, RhD typing and CAH may prove cost effective in comparison to later prenatal or postnatal treatment. When prenatal diagnosis is used to inform a termination decision, earlier

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does not cover a great majority of prenatal care. *Id.* The Children's Health Insurance Plan Reauthorization Act (CHIPRA) also now permits states to use CHIP federal matching funds to cover pregnant women who are above the income eligible for Medicaid coverage or above 185 percent of the federal poverty level, whichever is higher. *Id.*

129. KAISER FAMILY FOUNDATION, *supra* note 122, at 10. Medicaid coverage of births ranges state to state from 23 percent of births in New Hampshire to 63 percent of births in Louisiana. *Id.*

130. BARRY FURROW ET AL., HEALTH LAW 822–23 (6th ed. 2008).

131. KAISER FAMILY FOUNDATION, *supra* note 122, at 15.

132. *Id.* ACOG recommends that physicians offer all pregnant women, regardless of age, screening tests for Down syndrome and certain chromosomal abnormalities. ACOG also recommends that all pregnant women have the option of having a diagnostic test rather than a screening test for genetic and chromosomal abnormalities. ACOG Committee on Practice Bulletins—Obstetrics et al., *ACOG Practice Bulletin No. 77: Screening for Fetal Chromosomal Abnormalities*, 109 OBSTETRICS & GYNECOLOGY 217, 217–27 (2007).

133. KAISER FAMILY FOUNDATION, *supra* note 122, at 18.

134. Smith et al., *supra* note 27, at 632; Chachkin, *supra* note 124, at 43.

diagnosis can reduce the rate and severity of complications during an abortion, as the earlier a termination occurs, the lower the risk of complications.<sup>135</sup> If women decide to terminate prior to nine weeks gestation, they may elect to have a “medical” rather than surgical abortion, which also has lower complication risks.<sup>136</sup> Many private insurance plans cover both surgical and medical abortions, as well as any treatments that arise from complications during the procedure.<sup>137</sup> In the case of Medicaid, the Hyde Amendment prohibits the use of federal funds for abortion<sup>138</sup> except in the case of rape, incest, or when the mother’s life is in danger,<sup>139</sup> but states may elect to use their own funds to offer additional benefits. Thirty-two states do not offer funding for abortion beyond the federal level, but three of those have explicitly created an exception that permits the use of state funds for an abortion in the case of fetal abnormality.<sup>140</sup> Likewise, seventeen states and D.C. have gone beyond the federal minimum coverage guidelines and offer funding for all or most medically necessary abortions, medical or surgical.<sup>141</sup> Fewer complications and a reduction in surgical abortions can provide cost savings over current methods of prenatal diagnosis followed by pregnancy termination. For the reasons stated above, the state Medicaid programs and private insurance plans that do not currently cover prenatal genetic diagnosis may be more likely to do so once NIPD becomes commercially available.<sup>142</sup>

On the other hand, citizens in some states may voice significant moral opposition to Medicaid coverage of NIPD due to the perception that its use will increase abortion.<sup>143</sup> As a result, some state Medicaid programs may refuse to offer NIPD or will limit its use to a smaller set of conditions for political reasons related to protecting unborn life and narrowing the reasons for which a woman could seek an abortion. Bans on Medicaid coverage of

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135. Hall et al., *supra* note 102, at 249.

136. *Id.*

137. See Danco Laboratories, *Insurance and Medicaid*, EARLYOPTIONPILL.COM, [http://www.earlyoptionpill.com/section/health\\_professionals/insurance\\_and\\_medicaid](http://www.earlyoptionpill.com/section/health_professionals/insurance_and_medicaid) (last visited Dec. 1, 2010) (listing the coverage practices major insurers in sixteen states).

138. 42 C.F.R. § 441.200 (2010).

139. 42 U.S.C. § 1397ee(c)(1) (2006).

140. *State Policies in Brief: State Funding of Abortion Under Medicaid*, GUTTMACHER INSTITUTE (Feb. 1, 2011), [http://www.guttmacher.org/statecenter/spibs/spib\\_SFAM.pdf](http://www.guttmacher.org/statecenter/spibs/spib_SFAM.pdf).

141. *Id.*; Danco Laboratories, *supra* note 137 (stating Arkansas, Arizona, California, Connecticut, Illinois, Maryland, Massachusetts, Minnesota, Montana, New Jersey, New Mexico, New York, Oregon, Vermont, Washington, and West Virginia all offer some amount of coverage for medical abortions).

142. However, some states may limit the use of NIPD entirely or for certain conditions in order to limit the number of abortions that follow NIPD.

143. Chachkin, *supra* note 124, at 44.

NIPD in some states could significantly limit access to NIPD Medicaid recipients, further increasing health disparities between socioeconomic groups in ways that could have significant societal repercussions. If genetic diseases became largely associated with lower socioeconomic groups, discrimination against those with diagnosable genetic disorders could increase and the amount of societal resources for individuals living in society with those disorders could decline. As a society, we should strive to ensure that NIPD is offered on an equal basis to all pregnant women.<sup>144</sup>

Overall, however, NIPD offers many benefits over current prenatal and preimplantation genetic screening and diagnosis options to pregnant women, physicians, and insurance providers. These benefits will make physicians more likely to recommend NIPD, patients more likely to accept it, and public and private insurance providers more likely to cover it. Each of these factors will contribute to a substantial increase in the number of pregnant woman undergoing prenatal genetic testing.<sup>145</sup>

### *B. More Information*

In addition to the increase in women that will obtain diagnostic genetic testing, NIPD will significantly broaden the number of conditions for which prenatal diagnosis is both available and clinically appropriate.<sup>146</sup> The scope of current reproductive genetic testing is limited by both risk and expense. Prenatal genetic screening only provides relative risk information on a few serious conditions for which non-genetic biological markers exist, which greatly limits the number of conditions available for screening. Current prenatal screening programs include screening for neural tube defects, abdominal wall defects, SLOS, Down syndrome and Trisomy 18.<sup>147</sup> Physicians generally only offer IPD if a woman has a family history of a genetic or chromosomal disorder, screens high risk for a specific condition, or is high risk due to age or other medical condition.<sup>148</sup> The risks of IPD limit

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144. See Radhika Rao, *Equal Liberty: Assisted reproductive Technology and Reproductive Equality*, 76 GEO. WASH. L. REV. 1457, 1457–58 (2008) (for a thorough discussion of the importance of equality in reproductive rights).

145. See de Jong et al., *supra* note 80, at 273.

146. *Id.* at 272; Smith et al., *supra* note 27, at 633.

147. The California Prenatal Screening Program screens for neural tube defects, abdominal wall defects, Down syndrome, Trisomy 18, and SLOS, other programs may screen for fewer conditions. THE CALIFORNIA PRENATAL SCREENING PROGRAM, *supra* note 71.

148. Amniocentesis-Series, MEDLINE PLUS, [http://www.nlm.nih.gov/medlineplus/ency/presentations/100192\\_1.htm](http://www.nlm.nih.gov/medlineplus/ency/presentations/100192_1.htm) (last updated Sept. 2, 2009). *But see*, ACOG Committee on Practice Bulletins—Obstetrics et al., *supra* note 132, at 217–27 (recommending that

the appropriateness of performing the tests for less severe medical conditions, sex, behavioral and cosmetic traits in isolation, as medical ethics requires that the benefit of the information outweigh the risks of the procedure needed to obtain that information. In addition, few women would be willing to undergo the discomfort and expense of IVF and PGD without being high risk for a certain disease or condition.<sup>149</sup>

As a relatively inexpensive, non-invasive blood test, NIPD does not share these limitations. First, the benefit of nearly any kind of information would appear to outweigh the risks associated with performing the test.<sup>150</sup> Second, a number of start up companies already offer NIPD testing directly to consumers via the internet for a range of conditions, including RhD status and fetal sex.<sup>151</sup> These kinds of companies will likely offer testing for any condition for which there is consumer demand. Third, the availability of whole genome analysis from cffDNA from maternal blood serum will permit DTC companies and physicians to test fetuses for potentially hundreds of genetic diseases and all chromosomal abnormalities, as well as predispositions to other multifactorial conditions at the same time.<sup>152</sup> The ability to conduct a whole genome analysis of a fetus from a maternal blood

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physicians offer IPD to all pregnant women). However, at least one study suggests that ACOG's recommendation did not affect physician practice. Julie Reichling et al., Abstract, *Amniocentesis for Maternal Concern: The Impact of ACOG Guidelines*, 2010 ACMG ANNUAL CLINICAL GENETICS MEETING, available at <http://acmg.omnibooksonline.com/2010/data/papers/199.pdf> (last visited Feb. 19, 2010).

149. Common non-medical PGD uses include non-medical sex selection and HLA typing to ensure that the future child could be a blood and tissue donor for an existing sick child. Susannah Baruch et al., *Genetic Testing of Embryos: Practices and Perspectives of U.S. In Vitro Fertilization Clinics*, 89 FERTILITY & STERILITY 1053, 1055 (2008), available at <http://www.dnapolicy.org/resources/GeneticTestingofEmbryos.pdf> (showing that only 1 percent of PGD cycles—43 overall—in 2005 were initiated for HLA typing and 9 percent—320 overall—were initiated for non-medical sex selection).

150. See Smith et al., *supra* note 27, at 633.

151. See *Non-invasive Prenatal DNA Testing*, PRENATAL GENETICS CENTER, <http://www.prenatalgeneticscenter.com/gender-intro.asp> (offering sex determination at 10 weeks); *RhD Genotyping*, LENETIX MEDICAL SCREENING LABORATORIES, INC., [http://www.lenetix.com/html/rhd\\_sry\\_genotyping.html](http://www.lenetix.com/html/rhd_sry_genotyping.html) (offering RhD status at 15 weeks); *Prenatal Testing*, DNAPLUS, [http://www.dnaplus.com/prenatal\\_tests.htm](http://www.dnaplus.com/prenatal_tests.htm) (follow "Fetal Cell Prenatal Paternity Test" and "Fetal Cell Prenatal Gender Test" hyperlinks) (offering paternity testing at 13 weeks and sex determination 10 weeks); *FAQs About the DNA Gender Test*, CONSUMER GENETICS, INC., <http://www.consumergenetics.com/gender-test/boy-or-girl-faqs.php> (offering sex determination at 10 weeks); *Sending Samples to IBGRL*, THE BRISTOL INSTITUTE FOR TRANSFUSION SCIENCES, <http://ibgrl.blood.co.uk/ReferenceServices/RefSerSendSamples.htm> (offering RhD status at 16 weeks and sex determination at 7 weeks).

152. Lo et al., *supra* note 3, at 1.

sample means that the scope of genetic information available through NIPD will be limited only by our knowledge and understanding of genetics. The combination of genome-wide analysis and minimal risks associated with NIPD will mean that for nearly all genetic conditions a fetus' status will be both available and clinically appropriate to test for.

Some scholars have argued that this "specification creep"<sup>153</sup> may occur regardless of a shift from IPD to NIPD. In fact, because testing for multiple conditions at once would be possible through both technologies, one could argue that the invasiveness of the procedure would provide an incentive for parents to test for as many abnormalities or genetic conditions of interest as possible to justify the risk of testing and potentially termination.<sup>154</sup> For several years now, geneticists have been discussing the merits of broadening the scope of prenatal diagnostic testing, as genetic testing capabilities have improved.<sup>155</sup> Neither NIPD nor IPD requires a specific breadth of testing.<sup>156</sup> The scope can be determined on a patient-by-patient basis, set by practice guidelines for the profession, or established by policymakers.<sup>157</sup> However, regardless of whether clinicians offer a wide range of tests through IPD as well, an NIPD protocol will increase the number of women receiving testing for an expanded set of conditions. And as noted above, the societal impact of NIPD will depend on the combination of volume of women undergoing testing, the conditions for which they test, and how they use the information.

### C. More Actionable

How prospective parents use cffDNA test results will be a function of how "actionable" the information is, i.e., how it changes the options open to parents. Because NIPD is available so early in the pregnancy, its test results are more actionable than IPD results, as they offer more options for information gathering and treatment, as well as termination.<sup>158</sup> First, NIPD offers prospective parents more time to learn about the condition their fetus

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153. Wright, *supra* note 7, at 29; Hall et al., *supra* note 102, at 250.

154. See de Jong et al., *supra* note 80, at 274.

155. See *id.*; Caroline Ogilvie et al., *Current Controversies in Prenatal Diagnosis 3: For Prenatal Diagnosis, Should We Offer Less or More Than Metaphase Karyotyping?*, 29 *PRENATAL DIAGNOSIS* 11, 13 (2009); Evelynne Shuster, *Microarray Genetic Screening: A Prenatal Roadblock for Life?*, 369 *LANCET* 526, 528 (2007).

156. de Jong et al., *supra* note 80, at 274.

157. Reaching consensus on which conditions are appropriate for prenatal testing has been shown to be next to impossible and the regulatory challenges of doing so will be more fully discussed in Part IV.

158. Benn & Chapman, *supra* note 94, at 2155–56.

has, what support structures exist in society for individuals with that condition, and what life with an affected child would entail. In 2008, Congress passed the Prenatally and Postnatally Diagnosed Conditions Awareness Act, which aims to help women who receive a diagnosis of Down syndrome or other condition with “up-to-date information on the range of outcomes for individuals living with the diagnosed condition, including physical, developmental, educational, and psychosocial outcomes.”<sup>159</sup> Physicians could further supplement these requirements by providing pregnant women with information and resources to help them understand the realities of life for families living with disability. NIPD offers pregnant women significantly more time than current IPD protocols to make use of such resources and potentially connect with families of children with a similar diagnosis.<sup>160</sup>

Secondly, for women who would consider termination, more may choose to undergo NIPD because it offers diagnostic information at a point in the pregnancy when the termination options may be more tolerable both physically and emotionally.<sup>161</sup> Until nine weeks after the first day of her last menstrual period, a woman can have a medical abortion, as opposed to a surgical abortion.<sup>162</sup> In a medical abortion, the woman takes a combination of medications, usually misoprostal and mifepristone, to end the pregnancy and cause the uterine lining to shed.<sup>163</sup> Medical abortions are non-invasive and do not require anesthesia, and therefore a woman can take the medication and abort the fetus in her own home rather than in a clinical setting.<sup>164</sup> Even if a woman does not decide to terminate during the window when a medical abortion is possible, surgical abortions performed earlier in the pregnancy are less complicated and safer.<sup>165</sup> In contrast, surgical abortions performed after amniocentesis occur in the second trimester and require much more invasive procedures.<sup>166</sup> Dilation and Evacuation (D&E), the most common procedure

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159. PRENATAL TESTING AND DISABILITY RIGHTS 8 (Erik Parens & Adrienne Asch eds., 2000).

160. Benn & Chapman, *supra* note 94, at 2155–56.

161. In this section, I do not mean to suggest that women should find abortion more tolerable emotionally or physically, just that some women may find it more tolerable at an earlier time.

162. *Patient Education: Medical Versus Surgical Abortion*, UCSF MEDICAL CENTER, <http://www.ucsfhealth.org/adult/edu/abortion.html>.

163. *Id.*

164. *Id.*

165. Hall et al, *supra* note 102, at 249.

166. *Surgical Abortion Procedures – Dilation and Curettage*, AMERICAN PREGNANCY ASSOCIATION, [www.americanpregnancy.org/unplannedpregnancy/surgicalabortions.html](http://www.americanpregnancy.org/unplannedpregnancy/surgicalabortions.html) (last

performed after fourteen weeks, generally requires that the provider insert a synthetic dilator into the cervix for twenty-four hours prior to the procedure, which is then followed by the insertion of cone-shaped rods to continue the dilation process.<sup>167</sup> Once the woman is dilated, the provider places a tube into the uterus to suction out the majority of the fetal tissue, and then uses a curettage to scrape out any remaining contents.<sup>168</sup> Due to the increased risk to the woman during a D&E, it is usually performed in a hospital setting.<sup>169</sup> The safer and less invasive termination options offered by NIPD may make women more willing to engage in selective termination based on the genetic characteristics of their fetuses.

Further, early in the pregnancy, women may find an abortion more tolerable emotionally. Early in the first trimester, women have had less time to bond with the fetus or acclimate to being pregnant. The pregnancy may not feel “real” at that point. Many women wait until after 12-13 weeks to publicly announce their pregnancy, and are not physically showing their pregnancy until the end of the first trimester.<sup>170</sup> Many women may feel that the fetus has not developed to the point of becoming a “baby” by seven weeks, which may make abortion less psychologically traumatic at that time.<sup>171</sup> By fifteen weeks when amniocentesis becomes available, the pregnancy and the fetus have developed significantly. Women who undergo an amniocentesis generally have decided that they want a baby, but they are

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visited Aug. 3, 2011). Surgical abortions performed in the first trimester (prior to 13 weeks), known as suction curettage abortions, generally occur in a clinic or physician’s office under local anesthesia. UCSF MEDICAL CENTER, *supra* note 162. The physician inserts a tube into the vagina, through the cervix and uses suction from an electrical machine to empty the woman’s uterus. *Id.* Such an abortion could occur immediately after CVS, but since CVS is much less common than amniocentesis, the majority of abortions that result from prenatal genetic testing occur in the second trimester. *Surgical Abortion Procedures – Dilation and Evacuation*, AMERICAN PREGNANCY ASSOCIATION, [www.americanpregnancy.org/unplannedpregnancy/surgicalabortions.html](http://www.americanpregnancy.org/unplannedpregnancy/surgicalabortions.html) (last visited Aug. 3, 2011) [hereinafter *Surgical Abortion Procedures – Dilation and Evacuation*].

167. *Surgical Abortion Procedures – Dilation and Evacuation*, *supra* note 166.

168. *Id.*

169. *Id.*

170. *When to Announce Your Pregnancy*, BABYCENTER.COM, [http://www.babycenter.com/0\\_when-to-announce-your-pregnancy\\_10349769.bc](http://www.babycenter.com/0_when-to-announce-your-pregnancy_10349769.bc) (last visited April 15, 2012) (discussing the end of the first trimester as a “common time” for women to announce their pregnancy); Glade B. Curtis and Judith Schuler, *YOUR PREGNANCY WEEK BY WEEK* 89, 116, 155, 181 (5th Ed. 2004) (stating “you still probably won’t ‘show’” at seven weeks, “you still may not show much” at ten weeks, “your pregnancy may not be obvious to other people when you wear regular street clothes” at fourteen weeks, and “you are showing more now and have an obvious swelling in your lower abdomen” at seventeen weeks)

171. Hall et al., *supra* note 102, at 249.



concerned about the risk of disease or disorder.<sup>172</sup> For nearly four months leading up to the testing, the woman has been thinking about the pregnancy and bonding with the fetus. She is most likely showing and has probably shared the news of her pregnancy with others. All of these factors may make termination of an otherwise wanted pregnancy much more difficult.

The timing of NIPD may also change the calculus regarding what information is “actionable” with respect to selective abortion by broadening the scope of genetic conditions for which a pregnant woman would test.<sup>173</sup> The emotional and physical hardships associated with having a second trimester abortion or pregnancy loss may cause many women to either avoid IPD or to significantly limit the number of conditions for which they would test.<sup>174</sup> However, the availability of diagnostic genetic information at a time when a medical abortion is still possible may significantly lower many women’s threshold for prenatal genetic testing and expand the reasons for which they would selectively abort, resulting in an increase in pregnancy terminations overall.<sup>175</sup> For instance, parents who would not abort an otherwise wanted child at 18 or 20 weeks, because they preferred a different sex, may be more willing to do so early in the first trimester, thereby contributing to “specification creep.”<sup>176</sup>

More than any other advance in reproductive technology, NIPD has the potential to transform the way we think about pregnancy and our reproductive decision-making. No single feature of NIPD in isolation would make it revolutionary, rather it is the combination of factors and their interrelatedness that will be transformative. NIPD’s capacity to offer significant amounts of genetic information to prospective parents early in the pregnancy in a safe and relatively easy manner will contribute to physicians routinely offering it to all pregnant women as the standard of care.<sup>177</sup> While non-invasiveness is arguably the most important factor, the breadth of conditions for which testing will be possible and the early detection date will also increase both the use of diagnostic prenatal testing, as well as the potential reasons for fetal termination.<sup>178</sup> As Hall et al. suggest, “[m]ore

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172. Julie Chevalier Sapp et al., *Ambivalence Toward Undergoing Invasive Prenatal Testing: An Exploration of Its Origins*, 30 *PRENATAL DIAGNOSIS* 77, 77–82 (2010).

173. de Jong et al., *supra* note 80, at 274.

174. Smith et al., *supra* note 27, at 632–33.

175. de Jong et al., *supra* note 80, at 274; Benn & Chapman, *supra* note 94, at 2155; Kooij, *supra* note 99, at 167–68.

176. Smith et al., *supra* note 27, at 632–33; Wright, *supra* note 7, at 29.

177. Chachkin, *supra* note 124, at 24–38.

178. de Jong et al., *supra* note 80, at 274.

generalized use of non-invasive testing could facilitate selective terminations of pregnancy in a range of conditions hitherto not diagnosed prenatally and where the arguments for and against termination may not have sufficiently received scrutiny.”<sup>179</sup> While NIPD offers significant benefit over existing reproductive genetic testing, its widespread use raises concerns regarding its impact on patients, providers, and society as a whole. Medical ethicists and sociologists have begun to examine the implications of widespread NIPD use,<sup>180</sup> but the legal literature largely remains silent on both the short and long term challenges raised by NIPD use and the ways in which law and policy can be used to address them.<sup>181</sup> Part III will examine in depth two distinct challenges raised by the initial implementation of NIPD and offer a potential solution.

### III. INITIAL IMPLEMENTATION CONCERNS

Prior to widespread commercialization and integration of NIPD into prenatal care, two challenges must be addressed.<sup>182</sup> First, providers must decide what tests to offer. By removing the risks associated with current forms of prenatal diagnostic testing, NIPD lowers the threshold for appropriate genetic testing. However, the accuracy and reliability of many genetic tests remain unproven, while other tests offer little clinical benefit.<sup>183</sup> Unfortunately, few obstetricians have sufficient training in genetics or

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179. Alison Hall, Adam Bostanci & Stephen John, *Ethical, Legal and Social Issues Arising from Cell-Free Fetal DNA Technologies. Appendix III to the Report: Cell-Free Fetal Nucleic Acids for Non-Invasive Prenatal Diagnosis*, PHG FOUNDATION 1 (2009), available at <http://www.phgfoundation.org/search/?q=Ethicalpercent2C+Legal+and+Social+Issues+Arisin+g+from+Cell>.

180. Benn & Chapman, *supra* note 94, at 2155; Peter Benn & Audrey R. Chapman, *Ethical Challenges in Providing Non-invasive Prenatal Diagnosis*, 22 CURRENT OPINIONS IN OBSTETRICS & GYNECOLOGY 128 (2010); Hall et al., *supra* note 102; Schmitz et al., *supra* note 81, at 165; Dagmar Schmitz et al., *An Offer You Can't Refuse? Ethical Implications of Non-Invasive Prenatal Diagnosis*, 10 NAT. REV. GENETICS 515 (2009); Vardit Ravitsky, *Non-Invasive Prenatal Diagnosis: An Ethical Perspective*, 10 NAT. REV. GENETICS 733, 733 (2009); de Jong et al., *supra* note 80, at 234; Newson, *supra* note 75, at 103; Smith et al., *supra* note 27, at 631.

181. Chachkin, *supra* note 124, at 9; Hank Greely & Jaime King, *The Coming Revolution in Prenatal Genetic Testing*, 23 PROFESSIONAL ETHICS REP. 1 (2010).

182. Hall et al., *supra* note 102, at 249.

183. Gail H. Javitt, *Policy Implications of Genetic Testing: Not Just for Geneticists Anymore*, 13 ADVANCES IN CHRONIC KIDNEY DISEASE, 178, 179 (2006).

available time to identify those tests appropriate for NIPD.<sup>184</sup> Secondly, providers must decide what information to give patients regarding the tests offered. The advent of NIPD testing will place significant strain on our current practice of genetic counseling and informed consent for prenatal genetic testing, and will require a new paradigm of informing patients of the risks and benefits of engaging in prenatal genetic testing. Both the challenges involved in determining which tests to offer patients and what information to provide them with have the potential to create confusion, misinformation and problems for prospective parents and prenatal care providers attempting to use NIPD. This article proposes a single solution to both issues in the form of panels of genetic tests designated as meeting a threshold level of analytic and clinical validity and encompassing disorders with similar characteristics for genetic counseling purposes.

#### A. What Tests to Offer?

As our ability to offer a range of genetic test expands, minimum standards for tests offered through NIPD panels should be established.<sup>185</sup> As noted above, physicians have an ethical obligation to avoid engaging in a medical procedure for which the risks outweigh the benefits.<sup>186</sup> Historically, this obligation has limited prenatal genetic testing to a handful of well-researched, severe genetic conditions. For NIPD, the balance of risks and benefits changes significantly. In the absence of a significant risk to the fetus or mother, the benefit of added information—even imperfect information—will appear to outweigh the risks of testing. Unfortunately, with respect to many genetic tests, imperfect information abounds.<sup>187</sup> Neither the public nor physicians are well equipped to analyze the complexities of genetic interactions, laboratory testing methods, or the statistical risk factors required to determine the usefulness of many genetic tests.<sup>188</sup> As a result, the risk of false or misleading information may frequently go unacknowledged. In the realm of NIPD, this can have devastating results in the form of the

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184. *Id.* at 180; Marieke J.H. Baars et al., *Deficiency of Knowledge of Genetics and Genetic Tests Among General Practitioners, Gynecologists and Pediatricians: A Global Problem*, 7 GENETICS MED. 605, 605–10 (2005).

185. Benn & Chapman, *supra* note 94, 2155.

186. Tom L. Beauchamp & James F. Childress, *PRINCIPLES OF BIOMEDICAL ETHICS* 166 (5th ed. 2001).

187. Javitt, *supra* note 183, at 179; Benn & Chapman, *supra* note 94, at 2155.

188. Benn & Chapman, *supra* note 94, at 2155.

termination of an unaffected child, the birth of a child with a condition thought to be excluded, unnecessary anxiety, or general misinformation.<sup>189</sup>

According to the National Institutes of Health Secretary's Advisory Committee on Genetic Testing (SACGT), the benefits and risks of using any genetic test should be evaluated across four criteria: analytic validity, clinical validity, clinical utility, and social consequences.<sup>190</sup> Analytic validity is "how well a test measures the property or characteristic it is intended to measure."<sup>191</sup> Clinical validity indicates how well the test results correspond to the presence or absence of a clinical disease or predisposition.<sup>192</sup> Clinical utility refers to the usefulness of the information provided by the test to the patient or physician.<sup>193</sup> Finally, even analytically and clinically valid tests with high clinical utility may present negative social consequences in the form of discrimination for individuals receiving the test or living in society with stigmatized conditions.<sup>194</sup> Each of these four evaluative criteria should factor into a physician's decision to use a certain test for NIPD.

With respect to genetic tests, analytic validity means that the test accurately identifies the targeted sequence of nucleic acids.<sup>195</sup> In judging the analytic validity of a genetic test, providers currently have little information to go on. Regulating access to genetic tests based on analytic validity is typically left to the Center for Medicare and Medicaid Services (CMS) and the Food and Drug Administration (FDA), yet neither agency has taken an authoritative stance with respect to regulating genetic tests.<sup>196</sup> Through the Clinical Laboratory Improvement Amendments (CLIA), Congress granted CMS the authority to regulate diagnostic tests performed in clinical laboratories.<sup>197</sup> CMS requires laboratories that perform clinical tests within more complex areas of expertise, such as microbiology or diagnostic immunology, to obtain a specialty certification that requires minimum scores

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189. Smith et al., *supra* note 27, at 632.

190. NATIONAL INSTITUTES OF HEALTH, ENHANCING THE OVERSIGHT OF GENETIC TESTS 15, [http://oba.od.nih.gov/SACGHS/sacgt\\_documents.html#GT\\_DOC002](http://oba.od.nih.gov/SACGHS/sacgt_documents.html#GT_DOC002).

191. *Id.*

192. *Id.* at 11.

193. *Id.* at 12.

194. *Id.* at 20.

195. *Id.* at 15.

196. DEP'T OF HEALTH AND HUMAN SERVS., U.S. SYSTEM OF OVERSIGHT OF GENETIC TESTING: A RESPONSE TO THE CHARGE OF THE SECRETARY OF HEALTH AND HUMAN SERVICES, REPORT OF THE SECRETARY'S ADVISORY COMMITTEE ON GENETICS, HEALTH AND SOCIETY 29 (April 2008).

197. 42 U.S.C. § 263a(b) (2006) (requiring all laboratories that solicit or accept materials derived from the human body for laboratory examination to be certified).

on proficiency tests and quality assurance measures, as well as minimum training requirements for personnel.<sup>198</sup> However, CMS has not created a specialty certification for genetic testing.<sup>199</sup> Accordingly, there is, at best, little oversight of the analytic validity of genetic tests provided by any specific laboratory.<sup>200</sup>

In addition to CMS, the FDA also has the ability to regulate commercial use of any genetic test that qualifies as a medical device.<sup>201</sup> To the extent that a genetic test used for NIPD qualifies as a medical device under the Food and Drug Modernization Act by providing diagnostic information about a fetus, the FDA has the authority to determine whether the test meets safety and efficacy requirements needed for commercial use.<sup>202</sup> To date, the FDA has not exercised this authority to regulate most genetic tests.<sup>203</sup>

However, the agency seems more likely to begin regulating the safety and efficacy of genetic tests in the near future. In July 2010, the FDA held hearings to receive comments from stakeholders regarding how the government should oversee the validity and accuracy of genetic tests and other *in vitro* diagnostics.<sup>204</sup> As genetic testing becomes more prevalent in commercial markets, DNA microarrays are more widely used to test for multiple genetic mutations, and geneticists use complex statistical algorithms to evaluate those results in order to provide patients with diagnostic

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198. 42 C.F.R. §§ 493.801–493.807 (2010).

199. Javitt, *supra* note 183, at 178–79.

200. GAIL H. JAVITT & KATHY HUDSON, PUBLIC HEALTH AT RISK: FAILURES IN OVERSIGHT OF GENETIC TESTING LABORATORIES 4 (2006), *available at* <http://www.dnapolicy.org/images/reportpdfs/PublicHealthAtRiskFinalWithCover.pdf>.

201. 21 U.S.C. § 321(h) (2006). Section 201(h) of the Food, Drug and Cosmetic Act defines a medical device as “an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is . . . (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals.” *Id.*; *see also* U.S. FOOD & DRUG ADMIN. ET AL., DRAFT GUIDANCE FOR INDUSTRY, CLINICAL LABORATORIES, AND FDA STAFF: IN VITRO DIAGNOSTIC MULTIVARIATE INDEX ASSAYS 3 (2007), *available at* <http://www.fda.gov/cdrh/oivd/guidance/1610.pdf>.

202. Gregorio M. Garcia, *The FDA and Regulation of Genetic Tests: Building Confidence and Promoting Safety*, 48 JURIMETRICS J. 217, 226 (2008).

203. Baruch et al., *supra* note 149, at 7. The FDA does regulate certain components used in in-house laboratory tests, known as analyte specific reagents (ASRs), so that healthcare providers would know how the tests were being validated. *See* FOOD & DRUG ADMIN., *supra* note 201, at 3 (citing 21 C.F.R. §§ 809.10(e), 809.30, 864.4020 (2007)). *See generally*, Garcia, *supra* note 202.

204. Alla Katsnelson, *Consumer Genetic Testing in the Hotseat: A Week of Hearings Sows Uncertainty for the Fledgling Consumer Genomics Industry*, NATURE (July 29, 2010), <http://www.nature.com/news/2010/100729/full/news.2010.382.html>.

information on a range of conditions, the FDA will likely take a more active role in regulating the analytic validity of genetic tests.<sup>205</sup> However, how the FDA will go about regulating these multivariate arrays remains to be seen and will likely require deviation from its current protocols regarding medical devices.<sup>206</sup> The FDA did indicate that the level of regulation required will depend on the risk the specific test poses to the consumer, including the potential harm from an incorrect result.<sup>207</sup> This statement may indicate that the FDA intends to regulate access to genetic tests based on their usage as well as their accuracy.

While FDA guidance on analytic validity will be a step in the right direction, it will do little more than provide a minimum requirement for decisions regarding reproductive genetic testing. In examining a genetic test's overall efficacy, the FDA will hopefully also include information on the test's clinical validity. In general, genetic tests have high analytic validity, meaning they are highly accurate in measuring the presence of the particular DNA sequence of interest, but their clinical validity or the ability of the test to accurately predict the development of a condition of interest to the patient is less reliable.<sup>208</sup> Clinical validity analysis will reveal how closely associated the tested genetic sequence is with the onset of the disease or condition in question. In other words, if an individual has the gene sequence targeted by the genetic test, how likely is it that he or she will have the genetic disease or condition?

Information on this genotype/phenotype association is essential for deciding whether to offer a genetic test, and, unfortunately, it can be affected by many factors. First, a particular allele may be only one part of a multifactorial predisposition to disease; other genetic sequences or environmental factors and their interaction may also contribute to the presentation of the disease phenotype.<sup>209</sup> Second, an allele may have low penetrance, meaning that the presence of the disease genotype does not always result in the disease phenotype.<sup>210</sup> Low penetrance can even occur in

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205. *Id.*

206. *Id.*

207. *Id.*

208. NATIONAL INSTITUTES OF HEALTH, *supra* note 190, at 15.

209. Francis S. Collins et al., U.S. Nat'l Human Genome Research. Inst., *A Vision for the Future of Genomics Research: A Blueprint for the Genomic Era*, 422 NATURE 835, 840 (2003).

210. Human Genome Project, *Evaluating Genetic Tests: Some Considerations*, GENOMICS.ENERGY.GOV (Sept. 19, 2008), [http://www.ornl.gov/sci/techresources/Human\\_Genome/resource/testeval.shtml](http://www.ornl.gov/sci/techresources/Human_Genome/resource/testeval.shtml).

single gene disorders.<sup>211</sup> Finally, epigenetic factors, which are also controlled by other genes and the environment, can affect whether a gene is turned “on” or “off”, which would determine the phenotype.<sup>212</sup> Any one of these factors could cause an individual to receive a positive test result from a test with high analytic validity, but have a child who does not present with the phenotype of the tested for condition. A test with low clinical validity could cause a woman to abort a fetus that would never develop the genetic disease, causing needless heartache and loss.<sup>213</sup> While the FDA is determining how to regulate genetic tests, providers will be left to make choices on their own with little guidance. Unfortunately, most have little training in genetics and sparse understanding of the numerous factors that can affect the presentation of a genetic disorder.<sup>214</sup> Further, to properly make choices regarding which tests to offer, providers will have to know these factors for a wide array of genetic tests.

Rather than providers learning this information, biotechnology companies eager to get into the prenatal testing market are likely to make choices of what tests to offer for providers by creating genetic testing protocols. Existing companies, like Counsyl and 23&Me, currently offer pre-packaged genetic testing protocols that can be used for reproductive decision-making.<sup>215</sup> Counsyl, a genetic testing company in Silicon Valley, sells the Universal Genetic Test that enables prospective parents to know if a future child would be at risk for a recessive genetic disorder because both parents carry recessive alleles associated with the disorder.<sup>216</sup> The Universal Genetic Test offers diagnostic testing for over 100 of the most common recessive genetic disorders.<sup>217</sup> 23&Me also offers carrier screening for twenty-four genetic disorders to enable prospective parents to know if their

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211. *Id.* BRCA 1 and 2 are highly, but incompletely, penetrant, meaning that they cause a significantly increased risk for breast cancer, but do not guarantee the individual will contract the disease. *Id.* Scientists hypothesize that other mutations and environmental factors contribute to development of the disease. *Id.*

212. Elizabeth Pennisi, *Behind the Scenes of Gene Expression*, 10 *Sci.* 1064, 1064–67 (2001).

213. King, *supra* note 88, at 336; Garcia, *supra* note 202, at 232.

214. NEIL F. SHARPE & RONALD F. CARTER, *GENETIC TESTING: CARE, CONSENT, AND LIABILITY* 209 (2006).

215. *Counsyl*, COUNSYL.COM, <https://counsyl.com/> (last visited Aug. 11, 2011); *Health*, 23&ME.COM, <https://www.23andme.com/health/> (last visited Aug. 11, 2011).

216. COUNSYL.COM, *supra* note 215.

217. *Id.*

offspring are at risk of inheriting a genetic disease.<sup>218</sup> In addition, 23&Me sells a range of genetic testing protocols to satisfy consumer interest, including panels on ancestry testing, disease risk, and drug response.<sup>219</sup> Often the genetic tests offered as part of these protocols do not have the highest clinical validity, but instead offer imperfect information on conditions likely to be of interest to consumers.

DTC genetic testing companies are not subject to guidelines from the American Society for Reproductive Medicine (ASRM) or any other professional society regarding the appropriate uses of NIPD. Further, they do not owe their customers the same ethical and legal obligations that physicians owe their patients. In fact, their ethical obligations are almost entirely owed to their shareholders, which may incentivize the sale of tests for genetic conditions of great interest to the population, despite their lack of clinical validity or utility.<sup>220</sup> Given these risks, the challenges of communicating genetic risk information, the limited accuracy of certain genetic tests, and the extreme potential consequences of providing risk information in a prenatal context, some states may require physician involvement in NIPD testing, as many do with other laboratory tests.<sup>221</sup>

However, DTC companies have largely side-stepped that requirement by keeping physicians on staff to prescribe tests and offer limited forms of counseling.<sup>222</sup> Until the FDA provides a meaningful national approach to certifying the safety and efficacy of DTC genetic tests, state governments may be the only line of defense patients and consumers have against inaccurate or low utility tests. At a minimum, states should ensure that prospective parents receive NIPD for all medical tests under the guidance of an unbiased medical provider by passing laws or regulations that permit

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218. *Health-Carrier Status*, 23&ME.COM, <https://www.23andme.com/health/carrier/>. (last visited April 4, 2012).

219. *Ancestry*, 23&ME.COM, <https://www.23andme.com/ancestry/> (last visited April 4, 2012); *Health*, 23&ME.COM <https://www.23andme.com/health/> (last visited April 4, 2012).

220. See generally John R. Boatwright, *Fiduciary Duties and the Shareholder Management Relation: Or, What's So Special about Shareholders?* 4 BUS. ETHICS Q. 393 (1994).

221. CAL. BUS. & PROF. CODE § 1288 (2010). California was the first state to challenge DTC genetic testing companies by enforcing laboratory standards and requirements that patients receive tests through a licensed physician. Letter from California Health and Human Services Agency to Phil Robinson (June 9, 2008) (on file with author); GENETICS AND PU. POLICY CTR., SURVEY OF DIRECT-TO-CONSUMER TESTING STATUTES AND REGULATIONS (2007).

222. Alexis Madrigal, *23andMe to California: We're Not Ceasing or Desisting*, WIRED SCIENCE (June 24, 2008, 9:39AM) <http://www.wired.com/wiredscience/2008/06/23andme-were-no/>.



NIPD only under the guidance of an independent physician. While a physician may not have perfect clinical validity information, they do have a fiduciary duty to act in the patient's best interest.

Once clinical validity information becomes available, providers will be better equipped to determine the clinical utility of the test. The clinical utility of a genetic test measures the usefulness of the information for physicians and patients in making treatment choices. Clinical utility ranges from extremely high when the test results clearly dictate treatment protocol to very low if the results would not change the treatment protocol at all.<sup>223</sup> Many genetic tests will have a mid-range utility as they will inform a treatment decision, but other factors will also play a role. In the case of NIPD, test results can lead to prenatal treatment of the pregnant woman or fetus, preparation of the parents and physicians for the birth and care of an affected child, or a decision to terminate. Physicians should derive the clinical utility of a specific test from its known analytic and clinical validity, and use that information to determine which tests to include in NIPD. For example, they should avoid use of genetic tests when the analytic or clinical validity is so low as to negate the clinical utility of the test.

Finally, individual physicians may consider the social consequences in determining whether to offer certain tests in the prenatal context. For instance, some physicians may opt not to offer NIPD for non-medical sex selection, because they do not believe parents should terminate a fetus based on such information. While such a practice will not prevent prospective parents from accessing NIPD for such a reason, physicians may elect to exercise their personal autonomy in refusing to offer certain tests based on personal beliefs or potential social consequences. To this end, the Oklahoma legislature recently passed, over gubernatorial veto, a law prohibiting wrongful birth actions and in doing so protected physicians from liability for failing to disclose information that they believe might lead prospective parents to abort a fetus.<sup>224</sup> Twelve other states have similarly prohibited wrongful birth actions either by state court decisions or legislative action.<sup>225</sup>

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223. NATIONAL INSTITUTES OF HEALTH, *supra* note 190, at 12.

224. H.B. 2656, Reg. Sess. (Okla. 2010). See also Associated Press, *Oklahoma Senate Overrides Abortion Restriction Vetoes*, BOSTON HERALD, April 27, 2010, available at <http://www.bostonherald.com/news/national/southwest/view.bg?articleid=1250502>.

225. See Jillian T. Stein, *Backdoor Eugenics: The Troubling Implications of Certain Damages Awards in Wrongful Birth and Wrongful Life Claims*, 40 SETON HALL L. REV. 1117, 1131–32 n.92–93 (2010) (citing *Etkind v. Suarez*, 519 S.E.2d 210, 212 (Ga. 1999); *Grubbs v. Barbourville Family Health Ctr., P.S.C.*, 120 S.W.3d 682, 689 (Ky. 2003); *Taylor v. Kurapati*, 600 N.W.2d 670, 691 (Mich. Ct. App. 1999); *Wilson v. Kuenzi*, 751 S.W.2d 741, 746 (Mo. 1988); *Azzolino v. Dingfelder*, 337 S.E.2d 528, 537 (N.C. 1985); Idaho Code Ann. § 5-334(1)).

While most states do not have laws that could protect physicians from failing to disclose information they believe may lead prospective parents to seek an abortion, all states permit physicians to retain the ability to deny patients medical procedures they do not wish to perform.<sup>226</sup> As a result, some prenatal care providers may decline to offer NIPD for social reasons, which may limit access for certain portions of the population.

Unfortunately, understanding the analytic validity, clinical validity, clinical utility, and social consequences of a genetic test requires extensive knowledge and understanding of the underlying genetic disease, its characteristics, the cultural implications of the specific disease or condition, and the specific nature of the genetic testing process, which may be beyond the knowledge and understanding of many obstetricians seeking to determine whether a test is appropriate for NIPD. In addition, even physicians who have mastered this information may be unable to effectively communicate it in a manner that enables their patients to make an informed choice regarding whether they want to test their fetus for such a condition.

#### *B. How Should Providers Inform Patients?*

Historically, the main justification for engaging in prenatal genetic screening and testing is to promote the reproductive autonomy of prospective parents.<sup>227</sup> The decision to engage in prenatal screening or diagnosis carries significant weight and can have life-altering results. Establishing a method of informed consent for NIPD that adequately respects the range of prospective parents' desires for information while balancing the practical constraints of

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(LEXIS through 2009 Reg. Sess.); Ind. Code Ann. § 34-12-1-1 (LexisNexis, LEXIS through 2009 1st Reg. Sess. and 2009 Special Sess.); Mich. Comp. Laws Serv. § 600.2971(1) (LexisNexis, LEXIS through P.A. 2 of 2010 Legis. Sess.); Minn. Stat. § 145.424(1) (LEXIS through 2009 Reg. Sess.); Mo. Ann. Stat. § 188.130 (West, Westlaw through 95th Gen. Assembly, 1st Reg. Sess.); N.D. Cent. Code § 32-03-43 (LEXIS through 2009 Legis. Sess.); 42 Pa. Cons. Stat. Ann. § 8305(a) (West 2007); S.D. Codified Laws § 21-55-2 (Westlaw through 2009 Legis. of 84th Sess.); Utah Code Ann. § 78B-3-109 (LEXIS through 2009 1st Special Sess.)).

226. See American College of Obstetricians and Gynecologists, *ACOG Committee Opinion No. 385: The Limits of Conscientious Refusal in Reproductive Medicine*, 110 OBSTETRICS & GYNECOLOGY 1203, 1203–08 (2007); REPORT OF THE COUNCIL ON ETHICAL AND JUDICIAL AFFAIRS, CEJA REPORTS 6-A-07, AMERICAN MEDICAL ASSOCIATION (2007), available at [www.ama-assn.org/resources/doc/ethics/ceja\\_recs\\_6a07.pdf](http://www.ama-assn.org/resources/doc/ethics/ceja_recs_6a07.pdf) (last visited Aug. 11, 2010).

227. Schmitz et al., *supra* note 180, 515–16; SHARPE & CARTER, *supra* note 214, at 206.

physicians' and society's interests is of utmost importance, but will not be easy.<sup>228</sup>

The law generally requires health care professionals to inform the patient of the risks, benefits and alternatives to a proposed treatment and obtain her consent prior to commencing any treatment.<sup>229</sup> Ethical guidelines for prenatal genetic testing also recognize the importance of ensuring not only that the patient receives information on all relevant medical facts, but also that the patient engages in active decision-making and exercises a free choice to have testing.<sup>230</sup> Many scholars have expressed concern that without significant reconsideration of our informed consent procedures for prenatal diagnostic testing, many pregnant women will not make informed choices regarding the use of NIPD generally, testing for specific conditions, or selective abortion.<sup>231</sup> The following sections examine the current informed consent practices used for reproductive genetic testing, and why those practices are not well suited to informed consent for NIPD. I then propose a new model of informed consent for NIPD.

### 1. Current Informed Consent Practices in Reproductive Genetics

With respect to current prenatal genetic services, informed consent generally occurs in a two-step process.<sup>232</sup> First, the pregnant woman decides whether to engage in prenatal screening for risk factors associated with Down syndrome and other genetic and chromosomal disorders.<sup>233</sup> To make this decision, physicians and genetic counselors are advised to provide women with information on the available methods of prenatal diagnosis; the difference between screening (via ultrasound and maternal serum analysis) and diagnostic testing (via CVS or amniocentesis); the risks and benefits of

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228. Zuzana Deans & Ainsley J. Newson, *Should Non-Invasiveness Change Informed Consent Procedures for Prenatal Diagnosis?*, 19 HEALTH CARE ANALYSIS 122, 130–31 (2010).

229. Jaime S. King & Benjamin Moulton, *Rethinking Informed Consent: The Case for Shared Medical Decision-Making*, 32 AM. J. L. MED. 429, 439 (2006).

230. SHARPE & CARTER, *supra* note 214, at 207; CODE OF PROFESSIONAL ETHICS OF THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS § I at 5 (2008); AMA CODE OF MEDICAL ETHICS § 2.12 (1994).

231. Newson, *supra* note 75, at 105; Hall et al., *supra* note 102, at 249–50; Schmitz et al., *supra* note 180; Ananda van den Heuvel et al., *Will the Introduction of Non-Invasive Prenatal Diagnostic Testing Erode Informed Choices? An Experimental Study of Health Care Professionals*, 78 PATIENT EDUC. & COUNSELING 24, 24 (2009).

232. I will focus on the process for prenatal screening followed by amniocentesis, rather than that of CVS, as the majority of women pursue this process.

233. de Jong et al., *supra* note 80, at 273.

various techniques, including the risk of pregnancy loss associated with diagnostic testing; the timing of the procedures; details of the diseases and conditions for which the procedure screens or tests; the frequency of abnormal, false positive, and false negative results; the frequency of the need for repeat testing; the possibility that certain abnormalities may go undetected; and for newer procedures, a detailed explanation of their uncertainty and experimental nature.<sup>234</sup> Prior to engaging in prenatal screening, physicians should discuss with pregnant women which conditions they would like to be tested for and the different ways they could use the information, should they discover their fetus was at elevated risk for a genetic or chromosomal disorder.<sup>235</sup> This can have a variety of results. Some women will want as much information as possible. Others will want information, but decline screening because they would not want to undertake the risk of a miscarriage to receive diagnostic results should they screen high risk.<sup>236</sup> Others might decide that knowing their fetus was at higher risk might increase their anxiety levels for the rest of the pregnancy and opt against screening. Others still may want probabilistic information offered by a screening test, but not want to know for certain the status of her fetus, preferring instead to preserve hope that her child will not have a particular condition.<sup>237</sup> Some women, who would not consider terminating a fetus, might still want definitive diagnostic information to enable them to prepare for a potentially affected pregnancy. What is important is that pregnant women are given the opportunity to think through the implications of having risk information prior to engaging in prenatal screening.

Unfortunately, empirical research suggests that in many instances pregnant women do not receive any or all of this information prior to prenatal screening.<sup>238</sup> In practice, women often receive only limited

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234. SHARPE & CARTER, *supra* note 214, at 209.

235. *Id.* at 211.

236. E. García et al., *Reconsidering Prenatal Screening: An Empirical-Ethical Approach to Understand Moral Dilemmas as a Question of Personal Preference*, 35 J. MED. ETHICS 410, 412 (2009).

237. Deans & Newson, *supra* note 228.

238. Schmitz, et al., *supra* note 180, at 733; Nancy Press & C. H. Browner, *Risk, Autonomy, and Responsibility: Informed Consent for Prenatal Testing*, 25 HASTINGS CTR. REP. S9, S11–12 (1995); Cate Nagle et al., *Exploring General Practitioners' Experience of Informing Women About Prenatal Screening Tests for Foetal Abnormalities: A Qualitative Focus Group Study*, 8 BMC HEALTH SERVICES RES. 114, 118–19 (2008), available at <http://www.biomedcentral.com/1472-6963/8/114>; H-H Chiang et al., *Informed Choice of Pregnant Women in Prenatal Screening Tests for Down's Syndrome*, 32 J. MED. ETHICS 273, 274–75 (2006).

information before prenatal screening and due to the limited risks of the blood test, are rarely asked to provide informed consent.<sup>239</sup> As a result, women often remain unaware that screening may well lead to decisions regarding IPD and potentially pregnancy termination.<sup>240</sup>

In most cases, women receive prenatal genetic screening and then, only if they screen high risk, do they enter the second step of informed consent and genetic counseling.<sup>241</sup> If the fetus screens high-risk for a certain condition, providers can focus their discussion on that specific condition and provide extensive information on the child's prognosis. In addition, providers will also counsel prospective parents regarding the option of IPD to obtain more definitive information about the health of her fetus and the risk of miscarriage. At this stage, the importance of providing patients with clear, comprehensive information regarding the genetic condition of interest, the risks of testing, and time to reflect on it cannot be overstated. Due to the rarity of these disorders, many prospective parents will have little to no knowledge of the disorder or its impact, and therefore they will be "almost entirely dependent on their counselors for information about disabilities."<sup>242</sup> Unfortunately, many health professionals lack sufficient knowledge or resources to provide adequate information to prospective parents, especially as prenatal screening is increasingly performed as part of primary or obstetrical care, rather than via a geneticist.<sup>243</sup> An under-informed provider can greatly hinder a patient's decision-making capacity.

Timing is also important to the informed consent process.<sup>244</sup> A recent study on informed consent practices in prenatal testing revealed that 94 percent of practitioners surveyed believed that the offer and procedure of IPD should occur on different days.<sup>245</sup> This approach gives prospective parents the opportunity to reflect on their personal values and preferences prior to making a decision about whether to pursue further prenatal testing to receive a definitive result. Even with its flaws, prenatal screening followed

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239. Benn & Chapman, *supra* note 94, at 2154.

240. See *id.*; Valerie Seror & Yves Ville, *Prenatal Screening for Down syndrome: Women's Involvement in Decision-Making and Their Attitudes to Screening*, 29 *PRENATAL DIAGNOSIS* 120, 126–27 (2009).

241. Schmitz et al., *supra* note 180, at 733.

242. SHARPE & CARTER, *supra* note 214, at 208 (quoting THE ROYAL COMMISSION ON NEW REPRODUCTIVE TECHNOLOGIES, 2 *PROCEED WITH CARE: FINAL REPORT OF THE ROYAL COMMISSION ON NEW REPRODUCTIVE TECHNOLOGIES* 780–82 (Ottawa: Minister of Government Services 1993)).

243. *Id.* at 209.

244. Deans & Newson, *supra* note 228.

245. van den Heuvel, et al., *supra* note 231, at 27.

by IPD enhances the ability of genetic counselors and prenatal care providers to counsel patients regarding reproductive genetic testing. The minimal risk and non-diagnostic result associated with prenatal screening reduces the requirement for extensive counseling on the wide array of disorders screened for, but while still leaving clinicians the opportunity to provide extensive information on a single high risk disorder prior to diagnostic testing.

## 2. Informed Consent for NIPD

NIPD will not offer the same opportunities. Since its discovery, a handful of scholars have debated the effect widespread availability of NIPD will have on informed consent for prenatal genetic testing and reproductive autonomy.<sup>246</sup> Opinions range from the claim that NIPD represents an “ethical imperative”<sup>247</sup> required to promote reproductive autonomy to the concern that NIPD “might pose serious threats to the autonomous decision making of the pregnant woman”<sup>248</sup> to the notion that NIPD need not alter informed consent processes for prenatal genetic testing at all.<sup>249</sup>

Without question, NIPD offers significant benefits for prospective parents. First, by removing the risk associated with IPD, NIPD may reduce the ambivalence patients feel with respect to reproductive genetic testing, and therefore facilitate patients’ ability to make decisions based entirely on their personal values and preferences.<sup>250</sup> Further, NIPD will permit genetic counselors to focus on discussion of risks associated with the relevant genetic disorders, rather than those associated with IPD, improving the efficiency of counseling.<sup>251</sup> Second, providing pregnant women with more information about the genetic make up of their fetus will in many cases enhance their reproductive autonomy by expanding the range of conditions that can factor into their decisions. Finally, the timing of NIPD also increases women’s options and in turn bolsters her reproductive autonomy. In the instance that a fetus is affected by a genetic condition, being able to undergo

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246. Wright, *supra* note 7; Benn & Chapman, *supra* note 94; Benn & Chapman, *supra* note 180; Hall et al., *supra* note 102; Schmitz et al., *supra* note 81; Schmitz et al., *supra* note 180; Ravitsky, *supra* note 180; de Jong et al., *supra* note 80; Newson, *supra* note 75; Smith et al., *supra* note 27.

247. Ravitsky, *supra* note 180, at 733.

248. Schmitz, *supra* note 180, at 733.

249. de Jong et al., *supra* note 80, at 273.

250. van den Heuvel et al., *supra* note 231, at 27; Elizabeth Dormandy et al., *Attitudes and Uptake of a Screening Test: The Moderating Role of Ambivalence*, 21 PSYCHOL. & HEALTH 499, 500–01 (2006); Hall et al., *supra* note 102, at 249.

251. Ravitsky, *supra* note 180, at 733.

NIPD as early as nine weeks gestation leaves parents significant time to gather information on treatment options, life with an affected child, and the support services available. In contrast, amniocentesis frequently occurs close to the point of viability, leaving little time for such information gathering.<sup>252</sup> If the pregnant woman decides to continue the pregnancy, she has a greater amount of time to explore treatment options and prepare for the birth of a disabled child.<sup>253</sup> If she elects to terminate, termination will be safer, easier to obtain, and may be less emotionally traumatic.<sup>254</sup> Each of these factors will improve the ability of a pregnant woman to make a choice based on her feelings about having a child with a specific genetic condition, rather than other factors that currently must play into the decision.

On the other hand, concerns about NIPD's impact on reproductive autonomy stem from the probability that informed consent for diagnostic prenatal genetic testing will shift from a two-step process to a more general one-step process similar to consent for prenatal screening that compares the informational benefits of NIPD to the minor discomfort of having your blood drawn.<sup>255</sup> One study performed in the UK suggests that in this context offering NIPD may reduce disclosure, rather than expand it.<sup>256</sup> Ananda van den Heuvel and colleagues surveyed 231 health care professionals involved in prenatal testing regarding their informed consent practices using vignettes describing one of three genetic testing situations: IPD, NIPD, and maternal serum screening for Down syndrome (DSS).<sup>257</sup> The perceived need for a written informed consent varied significantly depending upon the type of test.<sup>258</sup> Ninety-six percent of respondents given the IPD vignette believed that testing should definitely or probably be preceded by a written consent, compared to 68 percent for NIPD and 73 percent for DSS.<sup>259</sup> Post-hoc analysis demonstrated that opinions about NIPD consent significantly differed from consent for IPD, but were similar to those about DSS, demonstrating that the miscarriage risk associated with IPD may be driving

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252. *Id.*

253. *Id.* (citing BZGA, EXPERIENCE OF PREGNANCY AND PRENATAL DIAGNOSIS 31, fig. 18 (Ilona Renner ed. 2006)), available at [http://www.bzga.de/botmed\\_13319270.html](http://www.bzga.de/botmed_13319270.html) (finding that 23.2 percent of women surveyed said prenatal diagnosis would enable planning and provision of care for the baby in good time in the event of a disability.).

254. *Id.*

255. Benn & Chapman, *supra* note 94, at 2155; Schmitz et al., *supra* note 180, at 515.

256. van den Heuvel et al., *supra* note 231, at 24.

257. *Id.* at 25–26. The majority of respondents were female (79.7 percent) obstetricians (59.3 percent). *Id.* at 26, tab. 1.

258. *Id.* at 27. ( $X^2 = 23$ ,  $df = 2$ ,  $p = .001$ ).

259. *Id.*

perceptions of the need for a formal consent process, rather than the diagnostic nature of the information contained in the test.<sup>260</sup> As a result, practitioners may fail to adequately consider the remaining implications of the testing procedures.<sup>261</sup> Patients may make the same mistake. Schmitz et al. have argued that removing the miscarriage risk will eliminate the psychological barrier that often forces patients and practitioners to make critical judgments about the risks and benefits of prenatal genetic diagnosis.<sup>262</sup>

Focusing only on the miscarriage risk ignores the fact that receiving diagnostic genetic information will not benefit all pregnant women.<sup>263</sup> For some, the information can be “toxic.”<sup>264</sup> Prenatal genetic tests, like other genetic tests, can have significant psychological ramifications. Prospective parents may experience guilt over passing a disorder to the fetus. They may feel guilt that their child is not affected, when other family members’ children are.<sup>265</sup> For late onset disorders, like Huntington’s Disease, prenatal testing of a fetus may also reveal that both the fetus and the parent will develop the disorder in the future, creating both guilt and anxiety for the prospective parent.<sup>266</sup> Prenatal genetic testing presents significant social and psychological risks, including anxiety, depression, and anger, that patients and providers should not overlook in deciding to test.<sup>267</sup> If patients and practitioners view NIPD as analogous to genetic screening rather than IPD, then some women will find themselves emotionally unprepared for and unintentionally facing a decision between termination and carrying an affected child to term.<sup>268</sup> Schmitz and colleagues argue that at this point, “reproductive autonomy would no longer be realizable, and the main ethical

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260. *Id.*

261. *Id.* at 25.

262. Schmitz et al., *supra* note 81, at 165.

263. Suter, *supra* note 125, at 233.

264. *Id.*

265. *Id.* at 237–38 (quoting Gail Geller et al., *Genetic Testing for Susceptibility to Adult-Onset Cancer: The Process and Content of Informed Consent*, 277 JAMA 1467, 1471 (1997)).

266. *Id.* (discussing the phenomenon that many individuals who knew they were at risk for HD did not want to undergo testing because they did not want to spend their lives waiting to develop the disorder).

267. *Id.* at 258–59.

268. Schmitz et al., *supra* note 81, at 165.



justification for non-invasive prenatal diagnosis would be reduced to mere rhetoric.”<sup>269</sup>

Other researchers have argued that a one-step approach to NIPD counseling does not necessarily make prenatal genetic counseling more difficult and ethically problematic.<sup>270</sup> Antina de Jong and colleagues claim that it is the expansion of the scope of prenatal testing that others assume will occur under NIPD that raises challenges for informed choice and reproductive autonomy, not the nature of the test itself.<sup>271</sup> Therefore if clinicians offered NIPD for only the conditions currently tested for under the two-step process of prenatal genetic screening followed by IPD, the challenges of adequately informing pregnant women are no different for NIPD than current testing.<sup>272</sup> While such an approach would reduce the potential for false or clinically unclear results, limit the amount of information and discussion necessary to adequately counsel patients, and lower the cost of both the procedure and the counseling,<sup>273</sup> the authors make two assumptions that are not tenable. First, this approach assumes that over time patients will not demand access to an expanded range of scientifically available genetic tests on which to make reproductive decisions.<sup>274</sup> Second, the approach assumes that health care providers can and do offer all necessary information on the conditions tested for during the first step of the two-step process. Empirical evidence does not support this assumption.<sup>275</sup> As discussed above, clinicians do not provide complete information prior to screening because doing so would be overly burdensome for them, anxiety provoking for patients, and potentially unnecessary at the point of screening. This is especially true when a second opportunity for a more in depth and particularized discussion exists, should one need to occur. As a result, the protocols for informing patients in a consistent and complete manner are not as firmly established as the authors suggest. Even for providers that do offer information on all conditions screened for in the first stage of informed consent, a second opportunity for discussion and clarification still exists prior to making a decision regarding diagnostic testing. NIPD alters this dynamic,

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269. *Id.* (citing V. Seavilleklein, *Challenging the Rhetoric of Choice in Prenatal Screening*, 23 *BIOETHICS* 68 (2009)).

270. de Jong et al., *supra* note 80, at 273.

271. *Id.*

272. *Id.* Dennis Lo has also echoed the sentiment that initially clinicians should limit NIPD testing to only those well-known and understood genetic disorders prevalent in certain populations. Lo et al., *supra* note 3, at 10.

273. de Jong et al., *supra* note 80, at 274.

274. *Id.*

275. See generally *supra* note 230; van den Heuvel et al., *supra* note 231, at 27.

and does so in a way that challenges our current informed consent process, even if used for the limited set of conditions currently screened for.

Providing sufficient information to enable a pregnant woman to make an informed choice about testing her fetus for numerous genetic conditions will require significant changes to either step in the current prenatal genetic testing informed consent process. Limiting the discussion to current practices for prenatal genetic screening would be inadequate.<sup>276</sup> However, offering comprehensive information for all genetic conditions similar to genetic counseling once an individual has screened high risk for a certain disorder to all women undergoing NIPD is impractical. First, there are insufficient numbers of genetic counselors and adequately trained obstetricians to accomplish this goal.<sup>277</sup> Second, the amount of time and information required to adequately counsel patients would make it burdensome on counselors and patients as well as prohibitively expensive.<sup>278</sup> Overall, NIPD has the ability to both improve and impede pregnant women's exercise of reproductive autonomy. If NIPD is introduced into clinical practice with little acknowledgment of the challenges it raises for informed choice, many women may receive genetic information about their fetus that they are unprepared for and would never have knowingly sought. However, if health care practitioners, genetic counselors, professional societies, ethicists and policy makers take this brief opportunity before NIPD becomes normalized in prenatal care to design informed consent guidelines specifically for NIPD, we can develop a practice that will permit NIPD to significantly enhance a pregnant woman's reproductive autonomy.

### 3. Two Step Consent Proposal

One possible solution is to require a two-step process for NIPD informed consent—one appointment for counseling followed by a second for decision-making and testing.<sup>279</sup> In van den Heuvel et al.'s survey, 94 percent of practitioners preferred patients to receive the offer and test on different days for IPD, whereas 74 percent preferred a two-step approach for NIPD and DSS.<sup>280</sup> Separating the offer and discussion of NIPD from the testing procedure differentiates NIPD from other routine laboratory tests given to a pregnant woman on her first prenatal visit and signifies the importance of

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276. Benn & Chapman, *supra* note 94, at 2154.

277. *Id.* at 2155.

278. de Jong et al., *supra* note 80, at 275.

279. Schmitz et al., *supra* note 180, at 733.

280. van den Heuvel et al., *supra* note 231, at 27.

thinking through the decision to engage in prenatal diagnostic testing. In a two-step approach, health care providers would first give patients information on the reliability of NIPD testing and the conditions tested for, then patients could take the information home, read it over, discuss it with the others close to them, and think through their values and preferences. At the second appointment, patients could ask any questions they had, discuss their thoughts with the practitioner, and decide whether to have the test. To expedite the process, the second appointment could be via telephone if the patient desired and afterward the physician could call the tests into the most convenient lab for the patient to have her blood drawn. The two-step process guarantees that the patient knows in advance that she is electing to undergo diagnostic prenatal testing and requires affirmative action by her to schedule and return for the testing. It also provides her with an opportunity to examine the information outside of the physician's presence and to discuss the decision with her spouse, family, or other interested parties.

A two-step approach raises some theoretical and practical challenges. Theoretically, providing patients with additional time to consider genetic testing may not produce more informed results and requiring two appointments may hinder access to desired treatment. Empirical evidence on the effectiveness of a two-step model is sparse. In the prenatal context, no empirical evidence exists to support or refute the assumption that providing patients with additional time for reflection facilitates informed choice.<sup>281</sup> While performing IPD counseling and testing on same day has been associated with higher rates of uptake, this practice has not been shown to be associated with making less informed decisions.<sup>282</sup> These findings may suggest that a two-step approach would reduce uptake without improving patient decision-making. However, these studies are very limited in number and scope and have not examined single step counseling in the context of NIPD. Other studies performed on the use of shared decision-making and clinical decision aids, which typically require a two-step approach,

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281. van den Heuvel et al., *supra* note 231, at 27.

282. *Id.*; Robert P. Lorenz et al., *Encouraging Patients to Undergo Prenatal Genetic Counseling Before the Day of Amniocentesis: Its Effect On the Use of Amniocentesis*, 30 J. REPRODUCTIVE MED. 933 (1985). One observational study even found that patients who received same day counseling and testing made more informed choices than those who separated counseling and testing, but this finding was not replicable in experimental testing. E. Dormandy et al., *Informed Choice to Undergo Prenatal Screening: A Comparison of Two Hospitals Conducting Testing Either As Part of a Routine Visit or Requiring a Separate Visit*, 9 J. MED. SCREEN 109, 109 (2002); E. Dormandy et al., *Informed Choice in Antenatal Down syndrome Screening: A Cluster-Randomized Trial of Combined Versus Separate Visit Testing*, 61 PATIENT EDUC. & COUNSELING 56, 56 (2006).

demonstrate improvement in the patient's knowledge and understanding of the decision and reductions in their decisional conflict.<sup>283</sup> In these studies, patients receive decision aids to take home and review with others prior to the meeting with their physician where the treatment decision is made. Clinical research is needed to determine the impact of a two-step consent process on the ability of individuals to make an informed choice regarding NIPD. Until the empirical research demonstrates that a single step approach provides similar levels of informed decision making and patient satisfaction, clinicians should err on the side of providing patients with more time for reflection and discussion.

Practically, a two-step approach creates more work for both provider and patient. Providers may have significant difficulty scheduling separate visits for information and decision-making for all of their prenatal patients. However, the use of phone appointments and nurse practitioners may help alleviate scheduling challenges. Secondly, providing the full extent of information required to enable a patient to make an informed decision regarding diagnostic genetic testing for a wide range of conditions will be nearly impossible to compile, let alone convey in an office visit, or even in an book of materials to take home. Patients are unlikely to read all of the relevant information on all genetic tests, even with extra time, and may still end up making uninformed decisions. A two-step informed consent process will offer women a chance to think through their decisions and ensures that they do not unwittingly undergo NIPD, but it will not remedy the sheer information burden associated with obtaining informed consent for NIPD for a wide range of conditions.

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283. Annette O'Connor et al., *Decision Aids for People Facing Health Treatment or Screening Decisions*, THE COCHRANE LIBRARY, no. 1, 2004. Of the 131 available decision aids examined in the meta-analysis, most were designed for use prior to counseling from a physician. Across the 131 trials decision aids for a variety of screening and treatment decisions, patients who used decision aids rather than usual care demonstrated: 1) greater knowledge; 2) more realistic expectations; 3) lower decision conflict; 4) increased patient activation; and 5) a smaller percentage of individuals undecided. *Id.* These findings were reconfirmed in the updated systematic review in 2009. Annette O'Connor et al., *Decision Aids for People Facing Health Treatment or Screening Decisions*, COCHRANE DATABASE OF SYSTEMATIC REVIEWS, no. 3, July 8, 2009, available at <http://www2.cochrane.org/reviews/en/ab001431.html> [hereinafter O'Connor et al., *Decision Aids 2009*].

*C. Proposal for NIPD Testing Panels and Corresponding Decision Aids*

To remedy challenges in selection of genetic tests appropriate for NIPD and informed consent, clinicians could offer NIPD in standardized panels that the patient selects based on their personal values and informational needs. Professional societies, such as the American College of Obstetricians and Gynecologists (ACOG), the National Society of Genetic Counselors (NSGC), and the American College of Medical Geneticists (ACMG) (the Professional Societies), with input from leading stakeholder groups should design testing panels appropriate for NIPD. Testing panels should be based on salient disease characteristics, in order to simplify informed consent for approved applications of NIPD.<sup>284</sup> For instance, inclusion of a test for a particular genetic condition on a panel should depend on the analytic validity, clinical validity, and clinical utility of the test, as well as characteristics of the condition, including age of onset, average life expectancy, severity of the symptoms, available treatment, and range of variation in symptoms. Different panels could exist to test for severe diseases with low life expectancy, diseases with significant cognitive and physical deficits and no treatment, diseases with significant cognitive and physical deficits and treatment, late onset disorders, predispositions to disease, and non-medical conditions, such as sex and other physical traits.

While diseases within each category will differ significantly from one another, many of the considerations for prospective parents may not. The distinctions between standard panels should highlight factors that have value for large portions of the population. For example, some parents may want to test for only those conditions that typically result in death before the age of five, where as others will want to test for serious mental and physical conditions, but not late onset diseases. Still others will want access to all available information. Standardizing panels will permit prospective parents to determine what kind of information they value and obtain only that kind of information. At the same time, standardized panels will permit genetic counselors to focus on the implications of certain categories of disorders in predictable ways, while avoiding having to discuss the implications of potentially hundreds of diseases and conditions.

In an effort to remedy the lack of genetic counseling resources, patient decision aids could be used to standardize the initial offer of information

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284. I do not recommend that Professional Societies determine what tests are available to the public, but that for those approved tests, they create approved panels of tests based on their salient characteristics.

regarding the various panels of tests available. Decision aids are videos and reading materials designed to convey standardized information regarding a medical decision to patients in an accessible manner.<sup>285</sup> Decision aids for NIPD panels would include detailed descriptions and salient features of the kinds of diseases tested for on a particular panel. Decision aids could also provide information from genetic counselors using a variety of methods to explain genetic risk information, and the possibilities of false positives and false negatives. In addition, these aids could present a range of values implicated by prenatal testing and in doing so offer an opportunity to change the discussion regarding having a child with a genetic disorder or disability on a national level.<sup>286</sup> They could include information on families living with a disabled child and their overall quality of life. Decision aids can prompt patients to consider their personal values with respect to prenatal genetic testing, including the kind of information they would want to know, and how they would use it. Patient decision aids often have patient testimonials that may help patients identify their own values or questions they may wish to discuss with their physician, family members, or other individuals with similarly affected children. After viewing the decision aid, patients who were still interested in receiving NIPD would have a follow up appointment or phone call with their provider to discuss the risks and benefits of testing for various panels. After an individualized protocol of panels has been selected and the provider answered any remaining questions, the woman would sign an informed consent form and go to the lab for testing.

This two-step consent/panel approach raises significant challenges. First, determining which tests should be on which panel will require difficult line drawing tasks. Placing a particular test on the severe disorders panel may send a message to prospective parents that there is an expectation that if their fetus tests positive for that disorder, they would abort. Whereas, if the same disorder were placed on the moderate physical or mental impairment panel, prospective parents may not feel the same pressure. Likewise, identifying certain disorders as severe for prenatal testing purposes may send the message that society does not value their lives as much as others.<sup>287</sup> As a result, the language used as part of the informed consent process must be very carefully crafted to avoid sending either of these messages. In many

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285. O'Connor et al., *Decision Aids 2009*, *supra* note 283.

286. For a more in depth discussion of the use of prenatal testing as an opportunity to reframe the existing discussion about disability, see Elizabeth Emens, *Framing Disability*, (draft on file with author).

287. Erik Parens & Adrienne Asch, *The Disability Rights Critique of Prenatal Genetic Testing: Reflections and Recommendations*, 29 HASTINGS CENTER REP. S1, S1–S2 (1999).

respects, creating decision aids may help standardize the message patients receive regarding living with disorders of this type and the fact that the decision to have an affected child remains a viable and socially supported option. Second, if not carefully tested prior to commercial use, decision aids may inadvertently bias patient decisions.<sup>288</sup> As with all decision aids, a national agency should be responsible for overseeing the creation of decision aids used for NIPD and testing them through clinical trials to ensure that they present all options, especially the option not to test, in a balanced manner. Finally, the use of testing panels may constrain the reproductive autonomy of prospective parents by forcing them to test for diseases and receive genetic information, which they otherwise would not want.<sup>289</sup> Two potential solutions exist. Providers can offer prospective parents the choice between a predetermined panel and an individualized set of genetic tests, which may cost significantly more. Alternatively, providers could permit patients to select the tests on the panel that they would like to see the results for and keep the results for the remaining tests confidential.<sup>290</sup> While this two-step/panel model presents some challenges, if the challenges are addressed properly, the benefits appear to outweigh the risks.

A two-step decision-making process that uses decision aids designed for predetermined panels of genetic tests based on similar characteristics accurately highlights the importance of the decision to engage in prenatal diagnostic testing, sends the message that testing is neither expected nor routine, promotes thoughtful reflection by patients, and limits the time and expense required to adequately inform patients. While such a process does not address all of the concerns with patient understanding and consent for NIPD, it will greatly improve the patient's chances of making an informed decision to engage in NIPD over existing prenatal genetic testing informed consent procedures.

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288. King & Moulton, *supra* note 229, at 490.

289. At the 2011 American Association of Law Schools Annual Meeting, Gaia Bernstein raised this criticism of genetic testing services like 23&Me and Counsyl, which offer testing for a range of conditions at once, but do not permit patients to individualize their testing. Gaia Bernstein, Professor of Law, Seton Hall University School of Law, *Genetic Testing*, Presented at THE ASSOCIATION OF AMERICAN LAW SCHOOLS ANNUAL MEETING (Jan. 6, 2011).

290. The latter approach raises significant ethical challenges, which are outside the scope of this paper, but should be explored in depth prior to implementing this model.

## IV. FUTURE SOCIETAL CHALLENGES FROM WIDESPREAD NIPD USE

As NIPD is introduced into prenatal care, we should consider what widespread NIPD use may mean for society as a whole. While NIPD will offer significant scientific improvements over current prenatal and preimplantation genetic testing techniques, does such testing raise any new questions regarding reproductive genetic testing in general? No, not really. For the last two decades, legal and ethical scholars have argued over what advances in reproductive genetic selection mean about our attitudes toward individuals living with disorders being screened for, the limits of individual reproductive autonomy, and the legal status of the embryo.<sup>291</sup> In general, most argue that while reproductive genetic testing offers significant benefits, its unconstrained use portends worsening of societal ills, including increased discrimination against individuals with undesirable genetic conditions, further socioeconomic stratification, and diminished autonomy with respect

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291. See, e.g., King, *supra* note 88; Sonia M. Suter, *A Brave New World of Designer Babies?*, 22 BERKELEY TECH L.J. 898, 922 (2007); FRANCIS FUKUYAMA & FRANCO FURGER, *BEYOND BIOETHICS: A PROPOSAL FOR MODERNIZING THE REGULATION OF HUMAN BIOTECHNOLOGIES* 293–300 (2006); June Carbone & Paige Gottheim, *Markets, Subsidies, Regulation, and Trust: Building Ethical Understandings into the Market for Fertility Services*, 9 J. GENDER, RACE & JUST. 509 (2006); Michael J. Sandel, *The Case Against Perfection*, 293 ATLANTIC MONTHLY 51 (2004); Rao, *supra* note 144, at 1457; JOHN A. ROBERTSON, *CHILDREN OF CHOICE* (Princeton University Press 1994); John A. Robertson, *Genetic Selection of Offspring Characteristics*, 76 B.U. L. REV. 421 (1996); Alexander N. Hecht, *The Wild Wild West: Inadequate Regulation of Assisted Reproductive Technology*, 1 HOUS. J. HEALTH L. & POL'Y 227 (2001); Michael J. Malinowski, *Choosing the Genetic Makeup of Children: Our Eugenics Past - Present, and Future?*, 36 CONN. L. REV. 125 (2003); Michael J. Malinowski, *A Law-Policy Proposal To Know Where Babies Come from During the Reproduction Revolution*, 9 J. GENDER, RACE & JUST. 549 (2006); Lars Noah, *Assisted Reproductive Technologies and the Pitfalls of Unregulated Biomedical Innovation*, 55 FLA. L. REV. 603 (2003); Adrienne Asch, *Why I Haven't Changed My Mind About Prenatal Diagnosis: Reflections and Refinements*, in *PRENATAL TESTING AND DISABILITY RIGHTS* 234 (Erik Parens & Adrienne Asch eds., 2000); Vicki G. Norton, *Unnatural Selection: Nontherapeutic Pre-implantation Genetic Screening and Proposed Regulation*, 41 UCLA L. REV. 1581 (1994); Erik Parens & Lori P. Knowles, *Reprogenetics and Public Policy: Reflections and Recommendations*, 33 HASTINGS CENTER REP. S1 (2003); Jennifer L. Rosato, *The Children of ART (Assisted Reproductive Technology): Can the Law Protect Them from Harm?*, 2004 UTAH L. REV. 57 (2004); Lindsey A. Vacco, *Pre-implantation Genetic Diagnosis: From Preventing Genetic Disease to Customizing Children. Can the Technology Be Regulated Based on the Parents' Intent?*, 49 ST. LOUIS L. J. 1181 (2005); Aaron R. Fahrenkrog, Note, *A Comparison of International Regulation of Pre-implantation Genetic Diagnosis and a Regulatory Suggestion for the United States*, 15 TRANSNAT'L L. & CONTEMP. PROBS. 757 (2006); Note, *Guiding Regulatory Reform in Reproduction and Genetics*, 120 HARV. L. REV. 574 (2006).



to reproductive choices. With NIPD, the substance of these issues remains the same, however, implementing NIPD into standard prenatal care, such that someday physicians might offer every pregnant woman a risk-free way to find out a great deal about her fetus' genotype at a very early point in the pregnancy, warrants serious reconsideration of these arguments. For the remainder of the article, I will briefly highlight some of the concerns resurfaced and expanded by routine NIPD use, which I hope will spur further discussion, research and writing in this area.<sup>292</sup>

Society as a whole should consider the social consequences of making NIPD for specific conditions part of standard prenatal practice. A routine offer of testing can send a message to patients that the physician views testing as a good idea and recommends it for a specific condition.<sup>293</sup> In addition, a routine offer of testing for a particular condition may also convey a belief that testing positive for such a condition justifies termination of a fetus. Indeed, the term "therapeutic abortion" conveys the idea that terminating the fetus is the "treatment" for its condition.<sup>294</sup> On a national scale, normalizing the offer of NIPD to all pregnant women can create significant pressure on women both to test their fetuses and terminate affected fetuses, as the information is easily available via a risk free medium.<sup>295</sup> This pressure can create a loop-back effect, such that the ease of testing and termination create disapproval for and reduction in support of women with disabled children, which, in turn, may increase the pressure to test.<sup>296</sup> The message may easily be distorted. For instance, Counsyl's website posts a quote from Steven Pinker, a professor from Harvard University, stating that "universal genetic testing can drastically reduce the incidence of genetic diseases, and may very well eliminate them entirely."<sup>297</sup> The website also claims "while these [genetic] diseases cannot be cured, with the Universal Genetic Test they can now be *prevented*. The test is recommended to be offered to both men and women and tests for diseases common to every ethnic group, for maximum safety."<sup>298</sup> Of course, the company fails to acknowledge that its test does not prevent the occurrence of a genetic

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292. I do not intend to begin to address any of these topics in the appropriate depth. My goal for this last section is to raise topics for future thought and discussion that I think are important issues with respect to the long-term implementation of NIPD.

293. Suter, *supra* note 125, at 241; de Jong et al., *supra* note 80, at 273.

294. Suter, *supra* note 125, at 266.

295. Schmitz et al., *supra* note 180, at 733.

296. Hall et al., *supra* note 102, at 249–50; van den Heuvel et al., *supra* note 231, at 28.

297. *What People Are Saying*, COUNSYL.COM, *supra* note 215.

298. *Introducing the Universal Genetic Test*, COUNSYL.COM, *supra* note 215.

disease, instead it prevents the birth of the person with the genetic disease. Seeking to “prevent” the birth of individuals with undesirable genetic traits is reminiscent of the eugenic goals of the early twentieth century.<sup>299</sup> Without significant thought and guidance, individual physicians and biotechnology companies may broaden the scope of reproductive genetic testing and selective termination without adequate consideration for the message sent to prospective parents or the social consequences of their collective action.

Routinizing NIPD into standard prenatal care creates the opportunity for collective individual parental decision-making to change the constitution of society. Francis Fukuyama and Franco Furger have argued that widespread use of reproductive genetic selection could lead to increased inequality resulting in a wide division between the “haves” and the “have nots.”<sup>300</sup> For instance, if private health insurance pays for NIPD, but Medicaid does not, this has the potential to accelerate the division. Further, Erik Parens and Adrienne Asch have argued that prenatal genetic testing and therapeutic abortion have the potential to negatively affect the way society perceives and treats individuals with undesirable genetic disorders and conditions.<sup>301</sup> Specifically, unfettered NIPD use has the capacity to lead to significantly more abortions of fetuses identified with certain genetic conditions and more abortions of fetuses for conditions currently not tested for prenatally.<sup>302</sup> But it does not have to.

We should ensure that the option to have a child with a genetic disorder remains a meaningful option. Whether this remains a reality will depend largely on the information pregnant women are given about NIPD and how it is framed.<sup>303</sup> The offer of NIPD not only represents an opportunity to help women make a decision regarding their own pregnancy, but it also represents an opportunity to educate a large portion of the population about the realities and positive aspects of the lives of individuals and families living with genetic disorders and disabilities. As a society, we must dedicate ourselves to offering comprehensive support services for families affected by a genetic disorder and to communicating the availability of those opportunities to parents who have recently had a fetus diagnosed with such a disorder. Significant barriers should be put in place to counteract the pressure to test and selectively abort affected fetuses that pregnant women may experience

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299. Judith F. Daar, *ART and the Search for Perfectionism: On Selecting Gender, Genes and Gametes*, 9 GENDER, RACE & JUST. 241, 260–61 (2005).

300. FUKUYAMA & FURGER, *supra* note 291, at 293–300.

301. Parens & Asch, *supra* note 287, at S1–S2.

302. Schmitz et al., *supra* note 180, at 733.

303. See generally Emens, *supra* note 286.

with respect to NIPD. The only way for NIPD to enhance prospective parents' reproductive autonomy is for it to truly broaden the options available to parents, rather than constrain them through increased social discrimination. Our ability to prevent the societal harms possible from widespread NIPD use will be determined by the actions we take from the outset to minimize the hardships associated with living in society with certain genetic conditions, monitor the collective decision making of individuals in society, and determine our overall societal goals associated with the use of NIPD.

Widespread NIPD may also cause us to reexamine states' abilities to restrict the free exercise of individual reproductive autonomy. If a woman can abort a fetus because she does not want any child, does the constitutional protection that affords her that choice extend to protect her ability to decide to abort a fetus for any specific genetic reason, even if the condition in question posed no or minimal clinical symptoms? We must consider whether reproductive liberty should protect the right of a woman to terminate a fetus because she does not want a child with a specific hair or eye color, or a predisposition to certain behavioral traits. Genetic testing companies will offer prospective parents this information, and many will accept. A recent study performed at New York University Medical Center found that around 10 percent of patients surveyed at the NYU Human Genetics Program for prenatal genetic testing would test for genes associated with non-medical traits such as longevity, superior intelligence, superior athletic ability, or height if they were available.<sup>304</sup>

In the interest of protecting unborn fetal life, states may attempt to restrict a woman's ability to abort based on information she discovered through NIPD. In fact, a handful of states have recently passed legislation restricting providers' ability to abort a fetus when he or she knows that the woman seeks the abortion based on the sex of the fetus.<sup>305</sup> The Arizona state legislature recently expanded the abortion prohibition to make it a class 3 felony to provide an abortion sought on the basis of the race or sex of the fetus.<sup>306</sup> These kinds of laws have significant practical and theoretical

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304. Feighanne Hathaway, Esther Burns & Harry Ostrer, *Consumers' Desire Towards Current and Prospective Reproductive Genetic Testing*, 18 J. GENETIC COUNSELING, 137, 137-46 (2009).

305. 18 PA. CONS. STAT. ANN. § 3204(c) (West 2000); 720 ILL. COMP. STAT. ANN. 510 / 6(8) (West 2003); H.B. 1595, 52nd Leg., 1st Sess. (Ok. 2009).

306. 2011 Ariz. Legis. Serv. Ch. 9 (West); Steven Ertelt, *Arizona: Brewer Signs Ban on Sex-Selection, Race-Based Abortions*, LIFE NEWS.COM (Mar. 30, 2011, 1:14 PM),

problems. Practically, they will be nearly impossible to enforce. Women seeking abortions for reasons of race or gender will be unlikely to reveal their reasoning to their provider. Theoretically, after a woman has undergone prenatal testing and discovered that her fetus has a genetic condition she does not want, a state may face significant constitutional challenges in forcing her to bear a child she does not want.<sup>307</sup>

But that is not the end of the story. A more serious challenge is whether a state can restrict the kinds of genetic tests available through NIPD for prenatal decision-making. If state governments cannot regulate a woman's ability to have an abortion for a specific reason, they may seek to regulate what prenatal and preimplantation tests a woman can have prior to viability to prevent parents from discarding fetuses for reasons the state deems not essential to reproductive autonomy. As a society, we will need to consider how to best balance an individual's desire to access all scientifically available information with the interest of a state to protect fetuses from being destroyed for trivial reasons.<sup>308</sup> Regulating access to these tests will not be easy. Many tests, such as fetal sex determination, serve both medical and non-medical purposes. And, as mentioned above, drawing lines regarding which tests are appropriate for NIPD use may negatively impact individuals living in society with the conditions for which screening will be available. Answering these questions will be challenging, but we must take the opportunity to consider the societal implications of widespread NIPD use, what kind of society we wish to live in, and how far to extend reproductive liberty. Many of these questions have been explored in depth in relation to other forms of reproductive genetic testing, but NIPD has the ability to affect the reproductive decision-making at a societal level making it imperative to reconsider these debates in the context of widespread NIPD.

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<http://www.lifenews.com/2011/03/30/arizona-brewer-signs-ban-on-sex-selection-race-based-abortion/?pr=1>.

307. A detailed analysis of the constitutional challenges surrounding a state's ability to regulate access to abortion or reproductive genetic testing is outside the scope of this article. For such a description, see Sonia M. Suter, *The "Repugnance" Lens of Gonzales v. Carhart and Other Theories of Reproductive Rights: Evaluating Advanced Reproductive Technologies*, 76 GEO. WASH. L. REV. 1514, 1576 (2008); Radhika Rao, *Reconceiving Privacy: Relationships and Reproductive Technology*, 45 UCLA L. REV. 1077, 1078 (1998).

308. I take up this issue in significantly more depth in a forthcoming article. Jaime S. King, *Not this Child: Constitutional Questions in Regulating Non-Invasive Prenatal Genetic Diagnosis and Selective Abortion*, 60 UCLA L. REV. \_\_\_\_ (forthcoming 2012).

## V. CONCLUSION

NIPD is coming, faster than our ability to fully consider the ethical, legal and social consequences of its use. Without question, NIPD offers prospective parents previously unimaginable benefits. Parents will have more knowledge about their fetus than ever before. Every year in the U.S., NIPD will prevent hundreds of women with wanted pregnancies from miscarriage caused by amniocentesis or CVS.<sup>309</sup> Prospective parents will avoid unnecessary treatment for diseases like RhD incompatibility, and be able to treat other genetic conditions while the fetus is still in utero or immediately upon birth. However, more than any advance in reproductive genetic testing, NIPD has the potential to dramatically change not only prenatal care, but also the way prospective parents think about their potential children. If offering NIPD testing for a wide range of conditions becomes the standard of care such that it is offered to a substantial number of pregnant women early in their pregnancy, prospective parents may view each pregnancy as “contingent” awaiting NIPD test results. We must take this brief moment to consider both the initial implementation challenges raised by NIPD, as well as the broader societal implications of its use. We have the chance to change our thinking about prenatal testing and the way it is presented to pregnant women. But such presentation must be done by careful design. Providers will need significant guidance and information on which tests to offer and how to best inform patients prior to engaging in NIPD. A two-step approach to informed consent that employs the use of decision aids and test panels created based on the salient characteristics of the underlying genetic conditions may significantly alleviate challenges faced in test selection and information transfer with patients. With respect to the broader social concerns, I have raised a number of potential issues in hopes of stimulating a societal conversation regarding the appropriate bounds of regulation and use of prenatal genetic testing in the future. I look forward to continuing to participate in this conversation as NIPD continues to enter the market.

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309. ABCNEWS.GO.COM, *supra* note 101.